

THE EPOXIDATION OF OLEFINS BY PEROXY COMPOUNDS

BY

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This dissertation is dedicated to my wife, Deise Prina Dutra, without whom I would never have started or completed it. It is also dedicated to my parents, Mario Joaquim Mateus and Emilia Maria Martins Mateus who always supported me and to the memory of Dr. Russell S. Drago, Doc, who was a source of continued enthusiasm for this work.

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Abstract of Dissertation Presented to the Graduate School
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The epoxidation of olefins is an important reaction due to the versatility of epoxides as intermediates in organic synthesis. The reaction can be performed using a variety of oxidants and activators. Great care must be taken in choosing reaction conditions to avoid opening of the oxirane ring, which is accelerated by the presence of acids. In this work the use of peroxy acids generated *in situ* for the epoxidation of olefins is described.

The formation of peracids by the reaction of a carboxylic acid and hydrogen peroxide is acid catalyzed. When this formation is done simultaneously with the epoxidation reaction in the presence of acids, epoxide yields are low due to ring opening. Peracids can also be formed by the reaction of carboxylic acid anhydrides and hydrogen peroxide, in which case an acid catalyst is not required. The use of phthalic anhydride for

the epoxidation reaction was studied. Hydrogen peroxide adducts such as urea-hydrogen peroxide were found to be beneficial to epoxide yields.

Peroxocarbonate species can be generated by the reaction of hydrogen peroxide and sodium hydrogen carbonate and are very active for the oxidation of thioethers. The epoxidation reaction was attempted using hydrogen monoperoxocarbonate generated *in situ*, under several different conditions. The solvent has to bring together the non-polar olefin and the aqueous solution containing the hydrogen peroxide and the sodium hydrogen carbonate. The counter-ion for the hydrogen carbonate was changed from sodium ion to a tetraalkyl ammonium ion to increase its solubility. The synthesis of the sodium hydrogen monoperoxocarbonate was performed and the compound was tested for the epoxidation of olefins. In all cases, no epoxide was produced by the peroxocarbonate species, due to the low nucleophilicity of the olefins.

The perhydrolysis in the presence of a base of a reactive ester such as methyl formate leads to moderate to good yields of epoxide. The neutral medium provided by the ester helps to avoid the opening of the epoxide ring and the carboxylic acid is neutralized by the base as the epoxidation proceeds. Sodium hydrogen carbonate was found to be an effective reagent for this reaction.

CHAPTER 1 THE EPOXIDATION OF OLEFINS

Introduction

The formation of epoxides from unsaturated hydrocarbons is a highly desirable reaction, for epoxides are widely used as building blocks in organic synthesis, as outlined in Figure 1.1.¹ Figure 1.1 shows a few transformations possible from the selective ring opening of epoxides. There are several methods for producing epoxides, both for large scale and fine chemical manufacture and the choice of method is normally connected with economic and reactivity issues. We can classify the diverse methods by the identity of the oxidant. Some processes use exclusively an organic oxidant while others require a combination of a transition metal catalyst and an oxidant. Peroxy acids, dioxiranes,² oxaziridines³ and oxaziridinium ions⁴ are all examples of organic oxidants able to perform the epoxidation reaction by themselves. Oxidants used in combination with a catalyst for olefin epoxidation include molecular oxygen, hydrogen peroxide, alkyl hydroperoxides, iodosyl benzene, sodium hypochlorite and peroxy acids.⁵⁻⁸

Dioxygen

Due to its low cost and very low environment impact, molecular oxygen should be considered the oxidant of choice. The selective oxidation of organic compounds by molecular oxygen remains, however, a challenge in many cases. To date, there are no

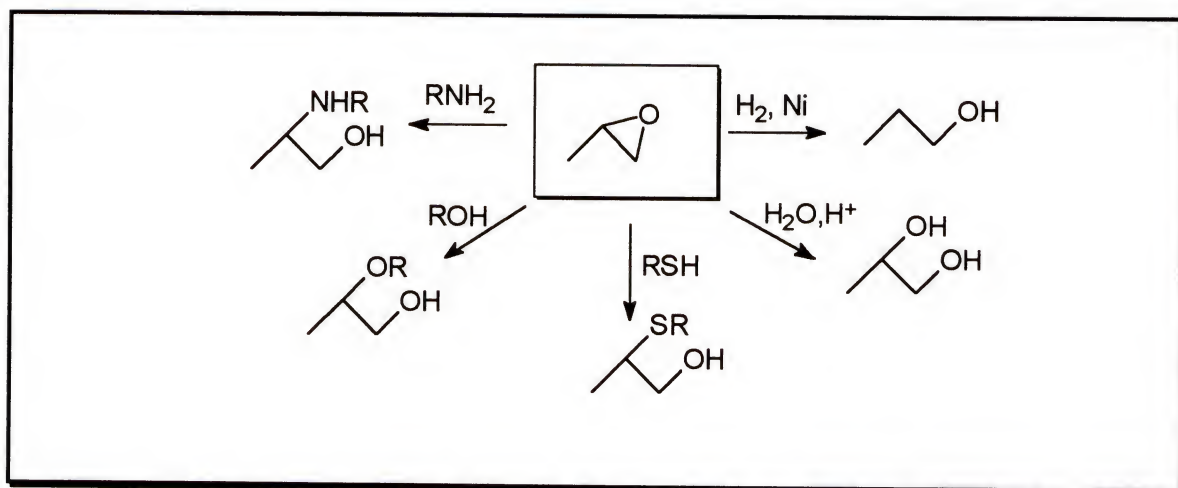


Figure 1.1. Synthetic routes using epoxides

commercial oxidation process using molecular oxygen other than those based on free-radical chain mechanisms.⁹ Due to the spin restriction of their respective ground states, there is a kinetic barrier to the direct reaction of O_2 (triplet ground state) with the organic substrate (singlet), which would otherwise be thermodynamically favorable. Once this barrier is overcome, it is often difficult to control the reaction, since the products being formed (alcohols, ketones, epoxides) are more reactive than the initial reactant. There are several ways to achieve the activation of O_2 and impose some selectivity to the oxidation process (Figure 1.2).

The coordination of dioxygen by metal complexes where a one electron higher oxidation state is available has been known for a long time.¹⁰ Figure 1.3 shows some of the different coordination modes of dioxygen to a metal center.¹¹ First row transition metals, such as iron and cobalt, often form metal-dioxygen complexes.¹² Cobalt complexes are normally used as model compounds to study oxygen coordination to hemoglobin.¹³

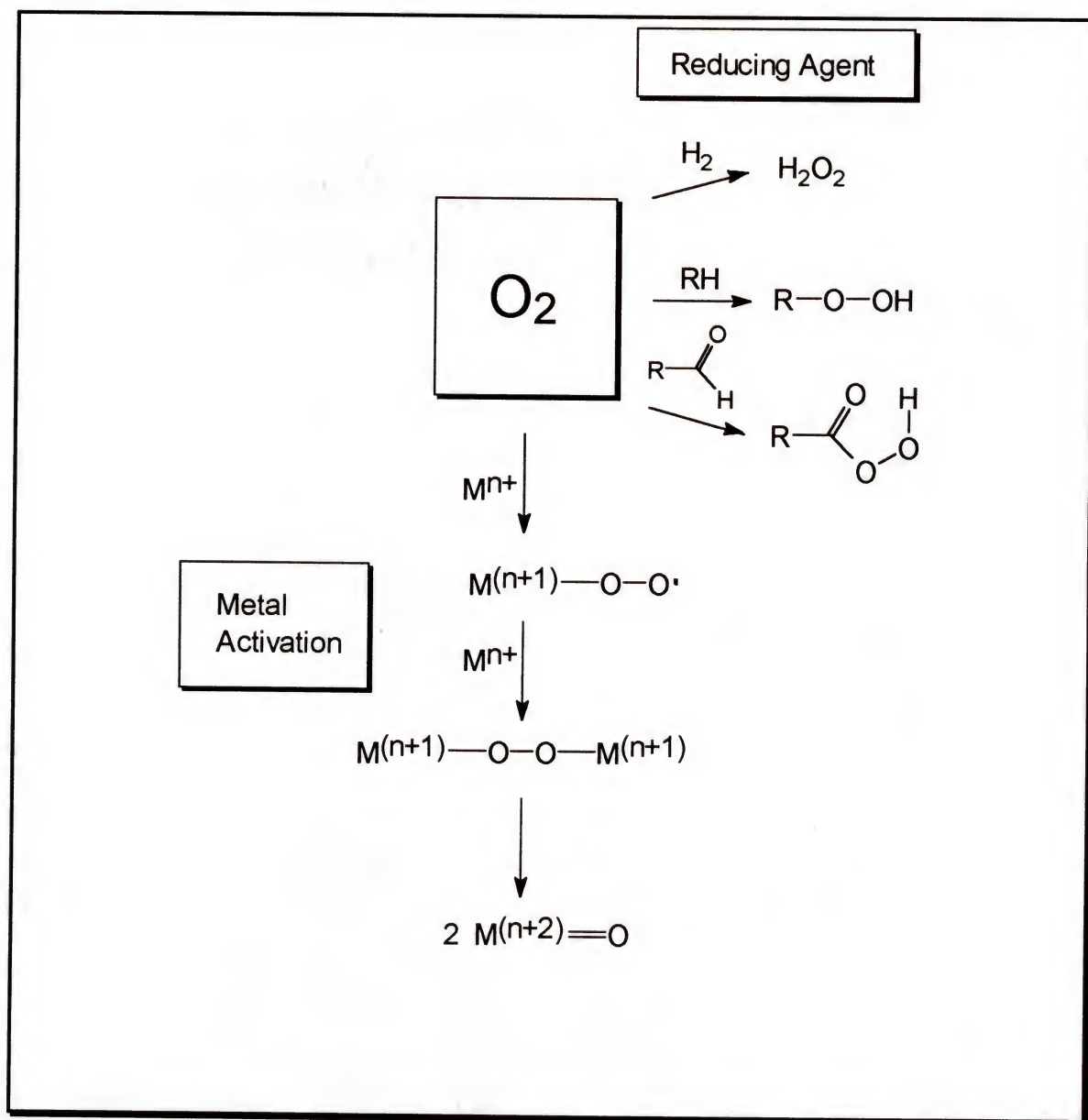
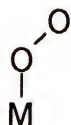


Figure 1.2. Routes for the activation of molecular oxygen

Mononuclear complexes

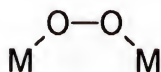


end-on (η^1)

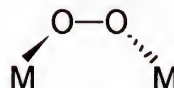


side-on (η^2)

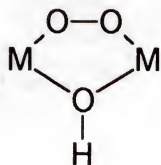
Binuclear complexes



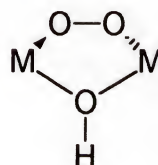
μ -superoxo (μ - $\eta^1:\eta^1$)
(usually planar)



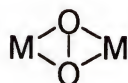
μ -peroxo (μ - $\eta^1:\eta^1$)
(usually non-planar)



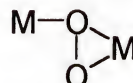
μ -superoxo μ -hydroxo
(usually planar)



μ -peroxo μ -hydroxo
(usually non-planar)



μ - $\eta^2:\eta^2$
bridged side-on



μ - $\eta^1:\eta^2$
mixed bridge

Figure 1.3. Coordination modes of molecular oxygen to metal centers.

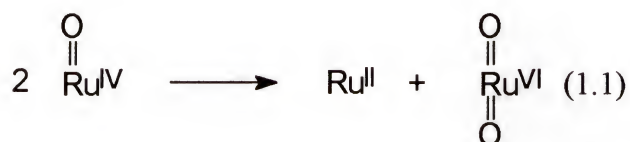
Drago and Corben¹⁴ proposed the spin pairing model to explain the coordination of oxygen to a metal center such as a cobalt (II) ion. In this model, the binding of O₂ is viewed as the combination of two radicals. The oxygen molecule is paramagnetic, with two unpaired electrons in the π -antibonding orbitals. These unpaired electrons can interact with the unpaired d-electrons in a metal complex having an empty or labile coordination position.

The amount of charge transfer from the metal to the dioxygen moiety is considered partial and is dependent on the orbital overlapping constants. This model contrasts with the ionic view of the O₂ binding, which dictates that a Co³⁺ and a superoxo anion (O₂⁻) are formed. These compounds are incapable of oxygen transfer, but are able to oxidize phenols through a hydrogen abstraction mechanism forming quinones and diphenoquinones.¹⁵ It has been found that coordination with the metal activates dioxygen by increasing its basicity (which increases hydrogen bonding with substrates such as phenols) and by increasing its radical character (which increases its reactivity with phenoxy radicals). This type of reaction, where oxygen is bound to a metal center, is known as a Class I reaction in Drago's classification scheme for homogeneous metal catalyzed oxidations by O₂.¹⁶ One serious limitation to the use of these types of complexes for the oxidation of other substrates, as in any hydrogen abstraction mechanism, is the strength of the R-H bond. Reaction will only occur if the M-OO-R bond formed is stronger than the R-H bond broken. For cobalt complexes the limit is estimated to be 90 kcal mol⁻¹.⁶

Unless sterically restricted, the metal-superoxo complex will dimerize, forming a μ -peroxo bridge. The μ -peroxo dimer can break forming two high valent oxo species

which can then perform the (ep)oxidation. Reactions that present this mechanism are classified by Drago as Class II reactions.¹⁶ Since both oxygen atoms will be transferred to the substrate this behavior is similar to the dioxygenase enzymes. Class II reactions have been observed in the case of porphyrin complexes of iron and ruthenium.¹⁷

Groves and Quinn observed the epoxidation of olefins by dioxygen in the presence of a ruthenium complex with a sterically hindered porphyrin such as tetramesitylporphyrin (TMP).¹⁸ The proposed mechanism involves the disproportionation of the $\text{Ru}^{\text{IV}}\text{O}$ into Ru^{II} and $\text{Ru}^{\text{VI}}\text{O}_2$ (1.1).



Drago and Bailey showed that the ruthenium oxo species containing the ligand 2,9-dimethylphenanthroline (dmp) are able to epoxidize olefins in the presence of molecular oxygen.¹⁹ Both $\text{Ru}^{\text{IV}}\text{O}$ and $\text{Ru}^{\text{VI}}\text{O}_2$ species were generated by oxidation of the ruthenium (II) (bis-aquo)(dmp) complex with cerium (IV). The reaction was specially selective for norbornene epoxidation and was performed in acetonitrile solution at 65°C and 3 atm of O_2 . The reaction presented an induction period where little or no epoxide is produced. This induction period did not disappear even if the catalyst was exposed to oxygen prior to substrate addition, implying that the substrate must be present for the formation of the active catalytic species. In the proposed mechanism,²⁰ an unusual peroxo complex containing both the metal and norbornene is suggested as an intermediate prior to the formation of the oxo species to account for these observations (Figure 1.4a). During the induction period, ketone and alcohol derived from norbornene are observed and these

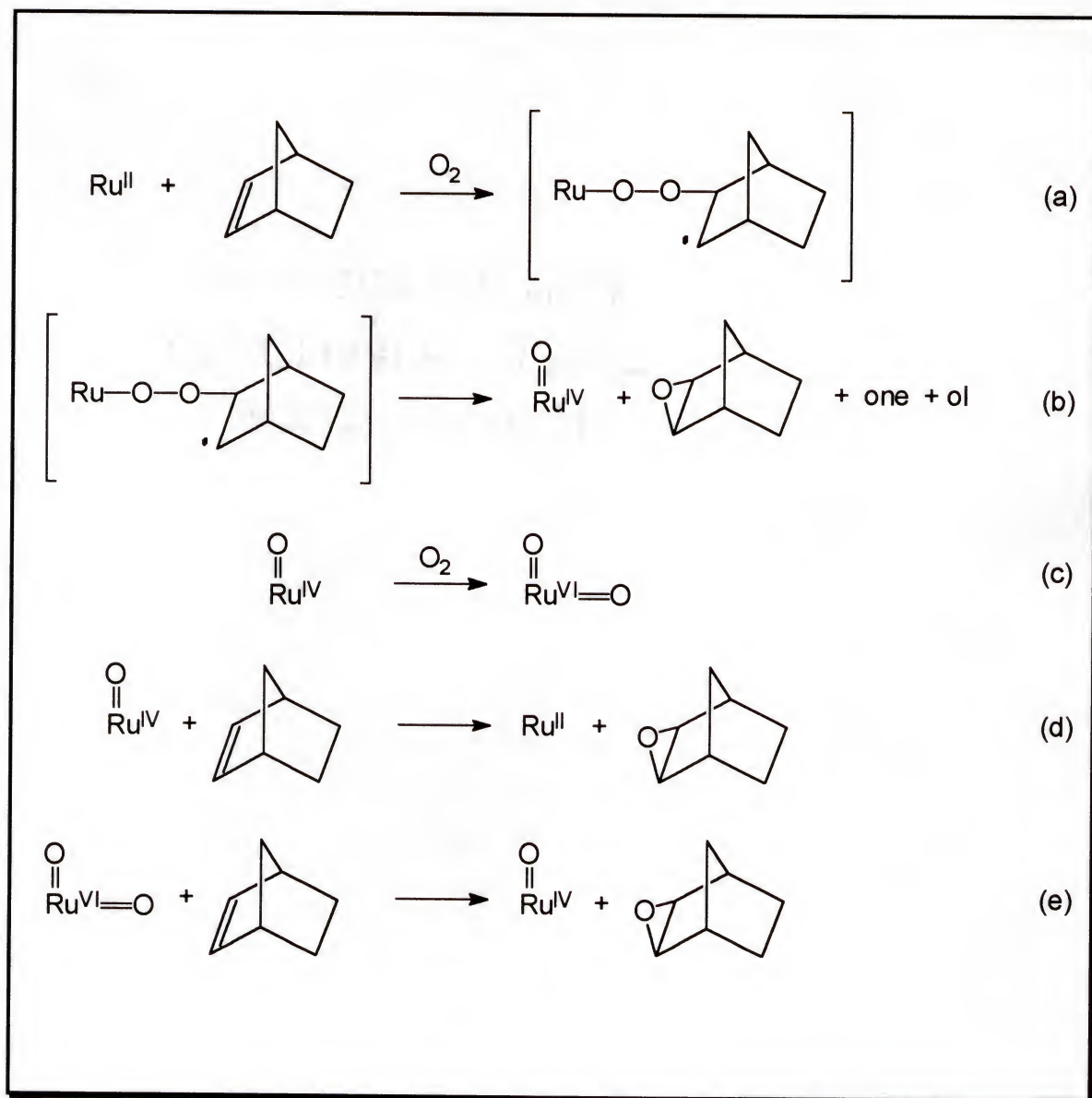
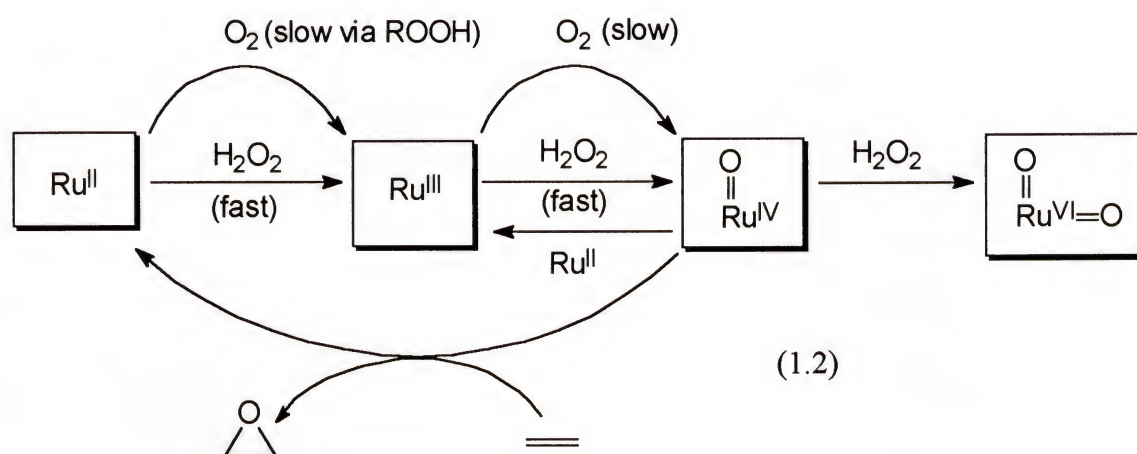


Figure 1.4. Mechanism for the epoxidation of olefins using $\text{Ru}(\text{dmp})_2(\text{H}_2\text{O})_2^{2+}$ and O_2 .

are typical products of a organic peroxide decomposition (Figure 1.4b). Once $\text{Ru}^{\text{IV}}\text{O}$ is formed, it is proposed to be oxidized to $\text{Ru}^{\text{VI}}\text{O}_2$ by O_2 (Figure 1.4c). The metal would then cycle between the (IV) oxo and the (VI) dioxo states, producing epoxide (Figure 1.4d and e). This complex was later used in the oxidation of alkanes.²¹

A more recent study proposed a modified mechanism, based on the redox chemistry of the system in water.²² It was suggested that Ru(III) slowly formed during the induction period. Molecular oxygen then oxidizes Ru(III) to Ru^{IV}O, which can, in turn, react with Ru(II) and generate more Ru(III). The Ru^{IV}O also reacts with olefin generating epoxide and returns the metal to the Ru(II) state. Once a certain concentration of Ru(III) is reached, the reaction becomes catalytic, maintaining a steady state concentration of Ru(III) (1.2).



Recent results have shown that the Ru(II) complex can be oxidized directly to Ru(III) by O₂ in H₂O, at 65°C.²³ This observation would imply that once a significant amount of Ru(III) is accumulated, disproportionation can occur generating the catalytically active species. More work is necessary to fully understand the autoxidation of the metal species in solution.

It is important to note that both Groves' and Drago's catalysts use sterically hindered ligands that prevent the formation of inactive μ -oxo dimers. In the case of dmp,

the ligand forces the *cis* conformation, avoiding isomerization of the di-oxo species to the more stable and less reactive *trans* form.

Direct activation of dioxygen by metal complexes without the use of a co-reductant is an unusual process. Supported silver catalysts can be used with dioxygen in the epoxidation of ethylene with very high conversions and selectivities. Promoters such as alkaline-metal and alkaline-earth carbonates are also used to avoid overoxidation (combustion). Even in the presence of such promoters the same catalysts will give very poor selectivities with higher olefins.

In a recent development,²⁴ the use of ruthenium containing compounds for the activation of dioxygen has been reported using polyoxometalates. A ruthenium substituted polyoxymetalate was able to epoxidize olefins and hydroxylate adamantane directly using O₂ without the need for a sacrificial reducing agent. The process does not involve a radical species and very good selectivities of the epoxide were obtained. The author speculates that the polyoxometalate cage protects the ruthenium from forming μ -oxo dimers in a similar fashion to that observed in the sterically hindered porphyrins and the 2,9-dimethylphenanthroline systems. A very comprehensive review on the catalytic properties of polyoxometalates and heteropolyoxometalates has been published recently.²

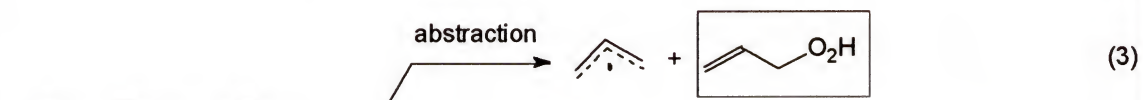
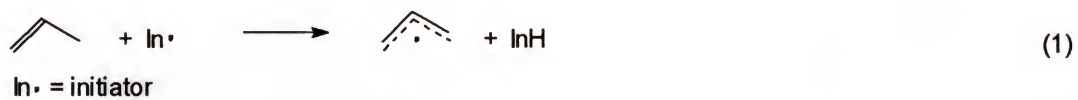
Even though the examples above show that direct activation of O₂ by metal complexes is possible, the most common method to activate molecular oxygen involves the help of a sacrificial reducing agent. When the reducing agent is hydrogen, hydrogen peroxide can form. Given the large number of processes involving the use of hydrogen peroxide in epoxidation reactions, they will be discussed separately.

An organic compound can function as the reducing agent in oxidation reactions.

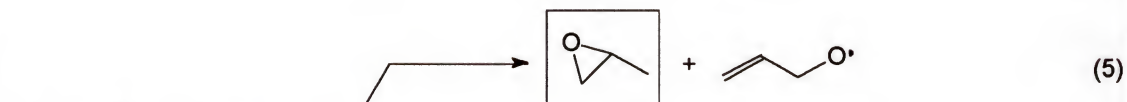
The oxidation of organic substrates by molecular oxygen is commonly referred to as autoxidation. This process involves a free-radical chain mechanism with the usual initiation, propagation and termination steps. When the substrate being oxidized is a saturated hydrocarbon, an alkyl hydroperoxide is generated which can be used for the oxidation of other organic compounds. The use of alkyl hydroperoxides in epoxidation will be discussed in a later section.

During the autoxidation of olefins, the chain propagation step can proceed through either abstraction or addition pathways, as shown in Figure 1.5 for propene. The radical formed in the addition step can decompose generating epoxide and an alkoxy radical. Since there are many other possible pathways, the selectivity of the reaction is generally low and will depend strongly on the olefin structure, the relative stability of the free radicals, and the oxygen pressure. One way to improve the selectivity of the autoxidation process is through the use of a second reagent which undergoes autoxidation more easily. Aldehydes are an important example of a substrate used in this type of two component system. The autoxidation of aldehydes generates acyl peroxy radicals which will prefer the epoxide generating route, as shown in Figure 1.6a. Chlorinated solvents such as CH_2Cl_2 or 1,2-dichloroethane give the best results. Recently it has been found that the reaction can be performed with good yields and selectivities in perfluorinated solvents.²⁵ This process takes advantage of the heightened solubility of O_2 in these inert solvents.

The autoxidation of aldehydes catalyzed by transition metal complexes (Figure 1.6b) has been used for the selective epoxidation of olefins. Since acyl peroxy radicals and



(4)



(6)

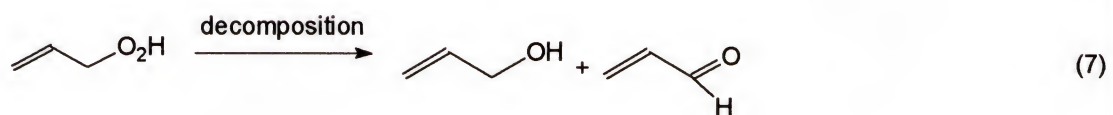


Figure 1.5. Examples of the autoxidation of olefins

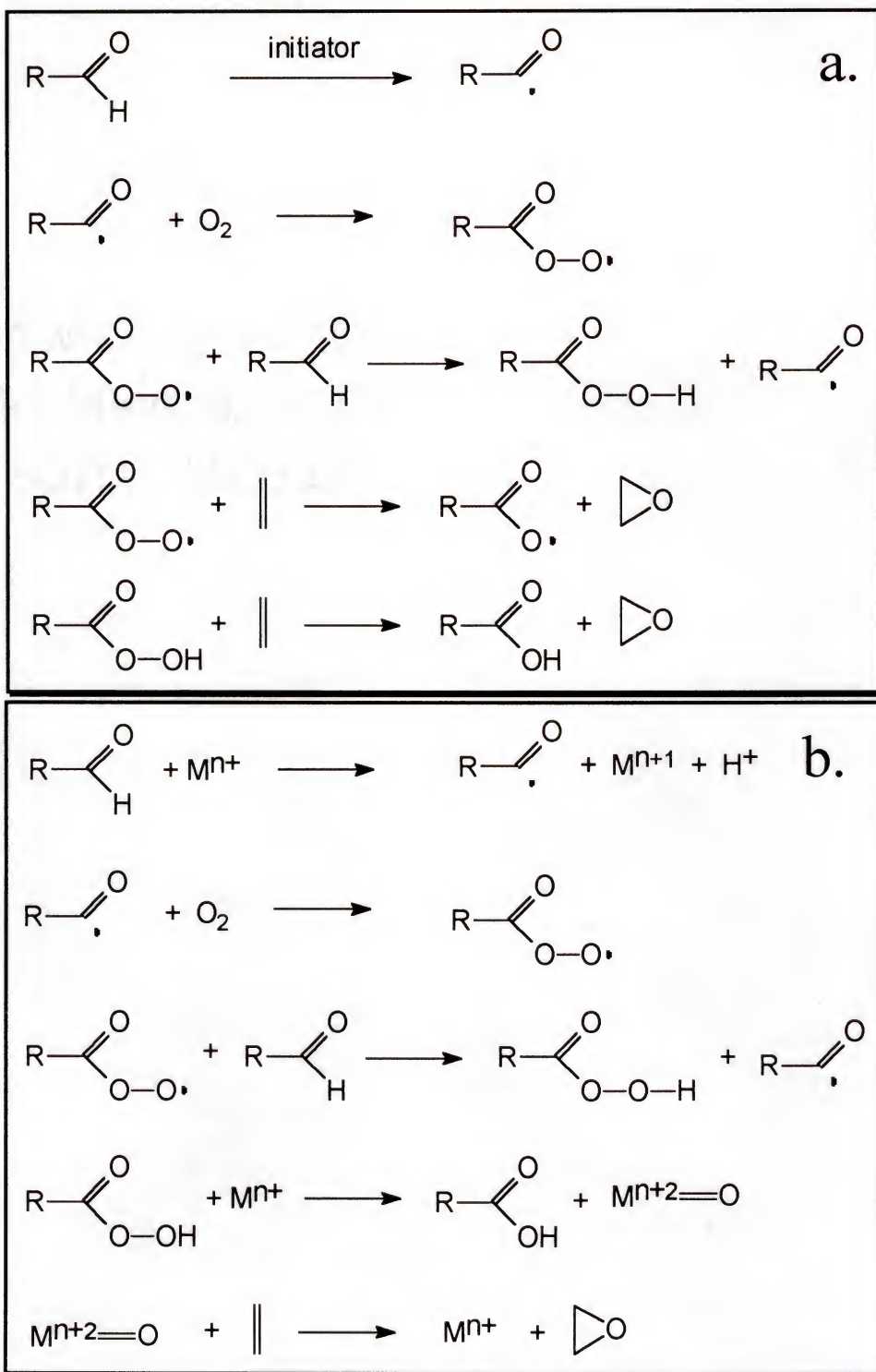


Figure 1.6. Autoxidation of aldehydes for the epoxidation of olefins. **a.** no catalyst. **b.** reaction catalyzed by metal complexes.

peracids are formed in this reaction, and these are able to perform the epoxidation by themselves, the importance of careful control experiments has been recently stressed.²⁶ One of the most compelling pieces of evidence suggesting that metal species do participate in the oxidation comes from the use of an enantioselective manganese catalyst. In the epoxidation of 2,2-dimethylchromene, the authors obtained the epoxide in 92% enantiomeric excess.²⁷ If the olefin epoxidation occurred following the peracid route, no enantiomeric excess would be expected. Alternatively, Valentine and co-workers²⁸ proposed that in the epoxidation of olefins using several first row transition metals with macrocyclic ligands, the metal functions mainly as a initiator of the free-radical process and that the acyl peroxy radicals are the primary epoxidizing agent.

Several systems have been recently reported which use a combination of molecular oxygen and aldehyde as oxidants for the epoxidation of olefins. Nickel (II) complexes have been found by Mukayama et al.²⁹ to epoxidize olefins in near quantitative yields when exposed to aldehydes and oxygen at room temperature. Porphyrins were used in another study as ligands for a series of metal ions (Cr^{3+} , Mn^{3+} , Fe^{3+} , Co^{2+} , Ni^{2+} , Cu^{2+} and Zn^{2+}) and the induction time and product distribution are highly dependent on the metal utilized and only complexes containing Mn^{3+} , Fe^{3+} , Co^{2+} and Ni^{2+} showed activity for epoxidation.³⁰

The monooxygenase enzyme cytochrome P-450 is another example of a very selective system which utilizes dioxygen, a sacrificial reducing agent and a metal catalyst. Only one of the oxygen atoms from molecular oxygen ends up in the oxidized species; the other one is reduced to water. Cytochrome P-450 enzymes oxidizes a variety of substrates, transforming them into more excretable or usable compounds. The active center of the enzyme contains an iron porphyrin. During the catalytic process, an iron

(III) metal center is oxidized by dioxygen in the presence of a reducing cofactor (NADH) to a formally $\text{Fe}^{\text{V}}\text{O}$ intermediate. The catalytic cycle is shown in Figure 1.7. The $\text{Fe}^{\text{V}}\text{O}$ species, a very strong oxidant, can be generated directly by the reaction of an oxygen donor such as hydrogen peroxide, a hydroperoxide or iodosyl benzene (PhIO). This "shortcut" in the mechanism is known as the peroxide shunt.

Hydrogen is an important reducing agent, normally used together with noble metal catalysts. Dioxygen can be used in conjunction with hydrogen gas and a heterogeneous catalyst for the epoxidation of olefins. Propylene oxide can be prepared by passing a mixture of propylene, hydrogen and oxygen through a supported gold catalyst at 300°C .³¹ The selectivity to the epoxide is 99 %, even though conversion is low. This can be compared to a similar catalyst containing platinum or palladium, where dissociation of the hydrogen molecule occurs and the hydrogenation product, propane, is the major product (92 % selectivity). The support of choice is titania in the anatase phase and the reaction appears to be very dependent on the identity of the support. No reaction is observed when rutile is used. The reaction also proceeds when large pore zeolites (MCM-41) are used as supports. Peroxo species formed on the interface of the gold clusters and the support may initiate the oxidation process.

Hydrogen Peroxide

Hydrogen peroxide is also an important oxidant and this substrate can be viewed as dioxygen activated by molecular hydrogen. There are several advantages to the use of hydrogen peroxide in oxidations. It is an environmentally friendly oxidant, yielding only water as the co-product, and it is commercially available as aqueous solutions up to 70 %

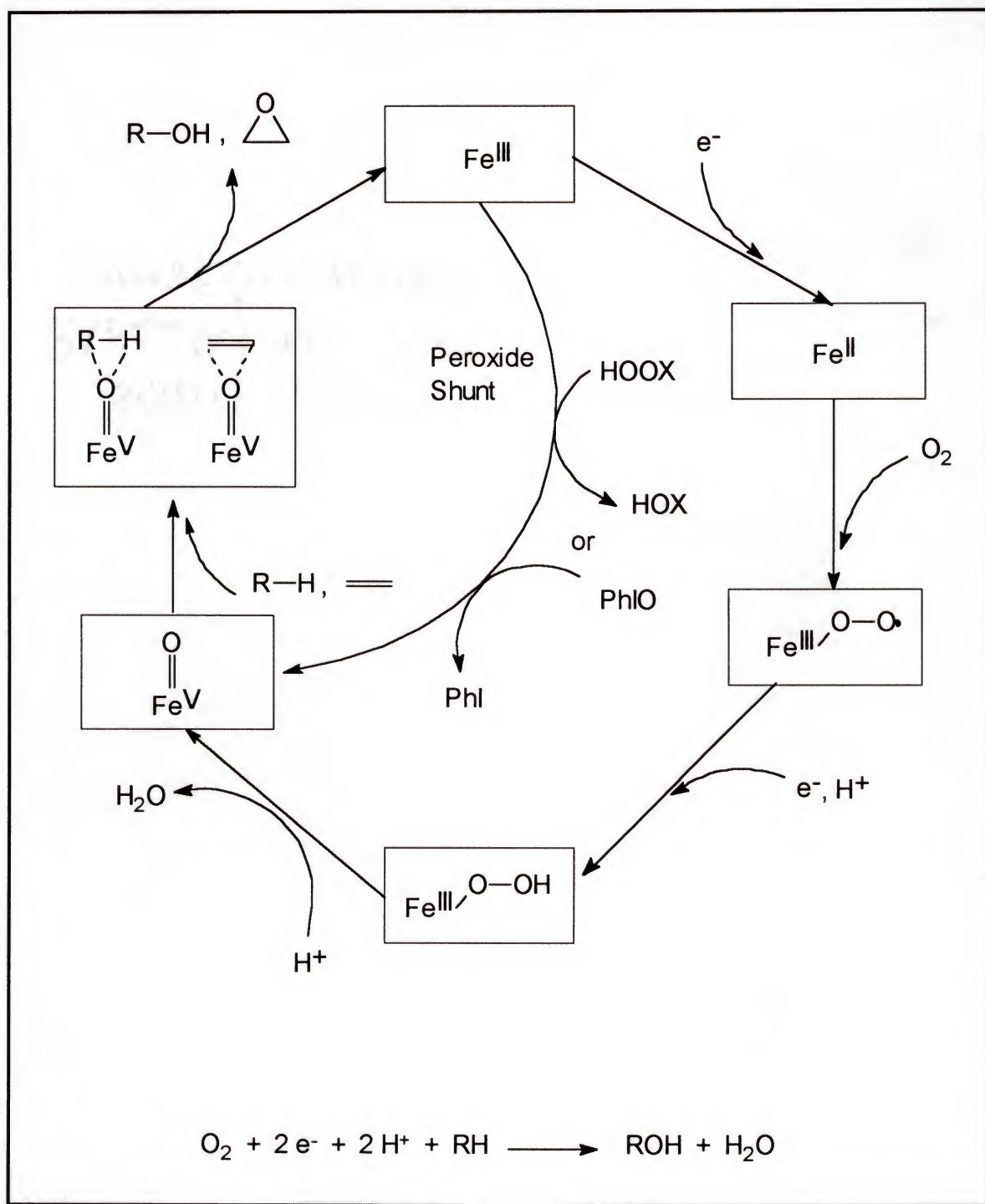


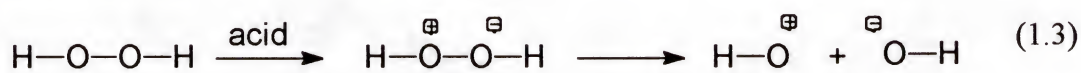
Figure 1.7. Mechanism of the oxidation of organic substrates by Cytochrome P-450

in weight. The primary drawbacks of hydrogen peroxide for large scale epoxide production are its cost and the losses associated with decomposition.

Hydrogen peroxide in most cases is not capable of performing epoxidations, and several methods to activate the molecule have been devised.³² The main activation methods include "direct" activation, activation through peracids or a metal catalyst, as displayed on Figure 1.8. The activator strongly influences the reactivity and the selectivity of the reaction.

The "direct" methods include cases where the peroxide molecule itself becomes the active species. Through the use of base, the perhydroxyl ion (HOO^-) is generated and it is a very potent nucleophile. The alkaline hydrogen peroxide method cannot be used for epoxidations of unfunctionalized olefins, but it is effective in the epoxidation of electron deficient olefins such as α,β -unsaturated ketones, of which quinones are a good example.³³

The second direct activation method involves the use of strong acids.³ Strong acids induce the polarization of the O-O bond which may result in the heterolytic cleavage of the hydrogen peroxide molecule (1.3).³⁴ The OH^+ generated from the cleavage acts as a powerful oxidant.



A thorough kinetic examination of the catalyzed epoxidation of cyclohexene by H_2O_2 in the presence of several strong acids (HClO_4 , H_2SO_4 , HPF_6 , HNO_3 and others) showed that the rate of reaction followed the strength of the mineral acids.³⁵ The authors

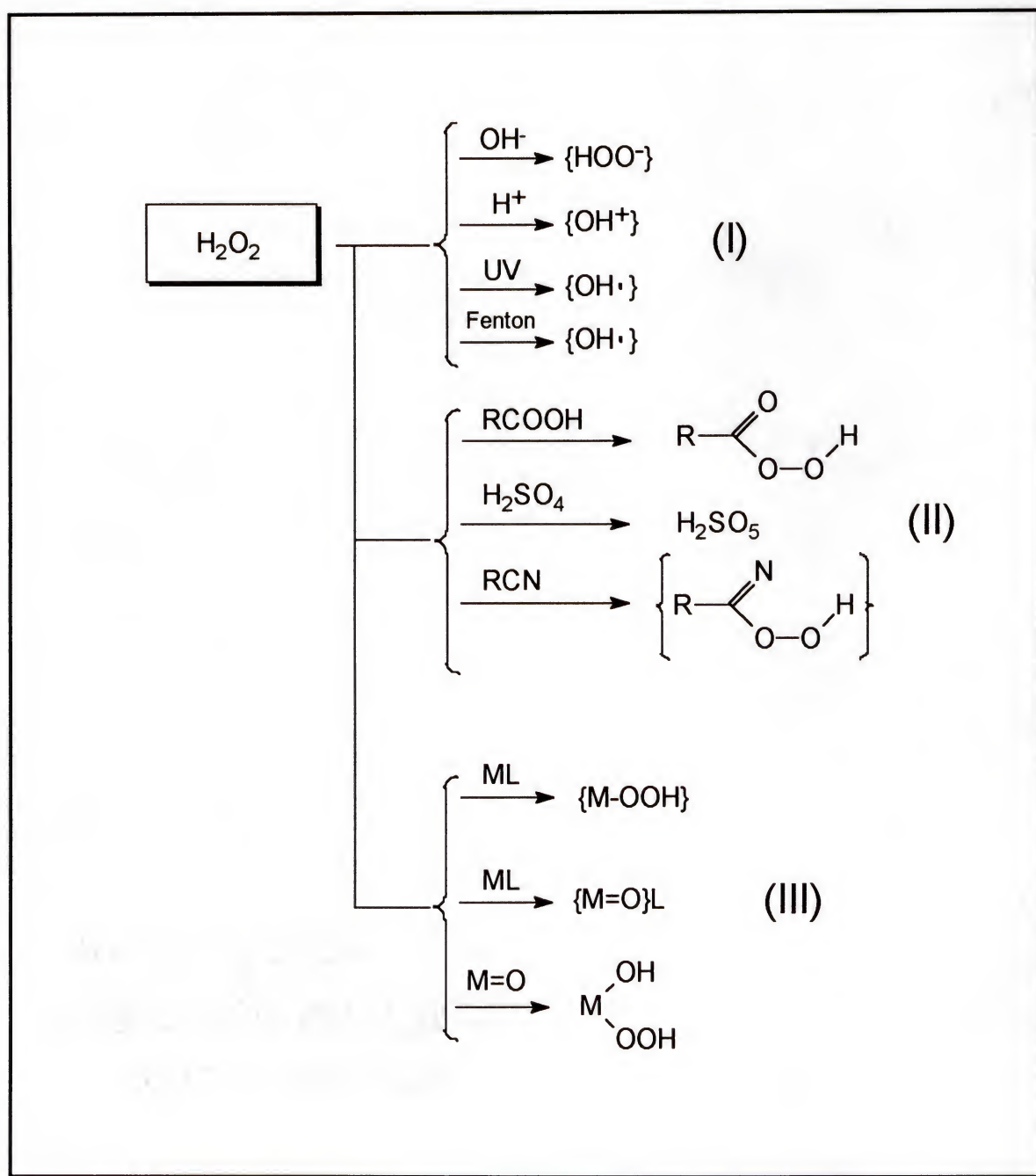


Figure 1.8. - Examples of methods for the activation of Hydrogen Peroxide (adapted from reference 3).

Species in brackets have not been isolated.

(I) - "Direct" activation

(II) - Activation via peracids

(III) - Catalytic activation

suggest that the protonated form of hydrogen peroxide, H_3O_2^+ , is the catalytically active species. For certain acids, the formation of a peroxy acid species is also possible.

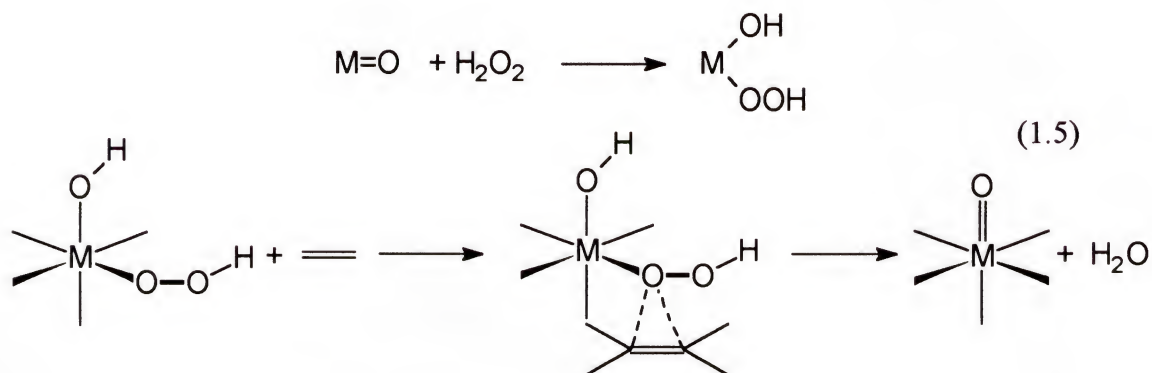
Generated through the homolytic cleavage of the peroxide molecule, the hydroxyl radical is also an extremely powerful oxidant. Ultraviolet (UV) radiation or a metal with a readily accessible higher oxidation state, such as the Fenton reagent (Fe^{2+}), can induce the homolytic cleavage of hydrogen peroxide.



The second category of hydrogen peroxide activators includes peracids or peracid-like species. The characteristics and the use of in-situ generated peracids in epoxidation will be discussed in Chapter 2.

The third and final category of hydrogen peroxide activators includes species that involve transition metal catalysts. Depending on the metal employed, these transformations can go through a homolytic or heterolytic mechanism.

Metals having low oxidation potentials and high Lewis acidity such as W, Mo, Ti and V epoxidize olefins through a heterolytic mechanism. The active species contains the metal in its highest oxidation state.

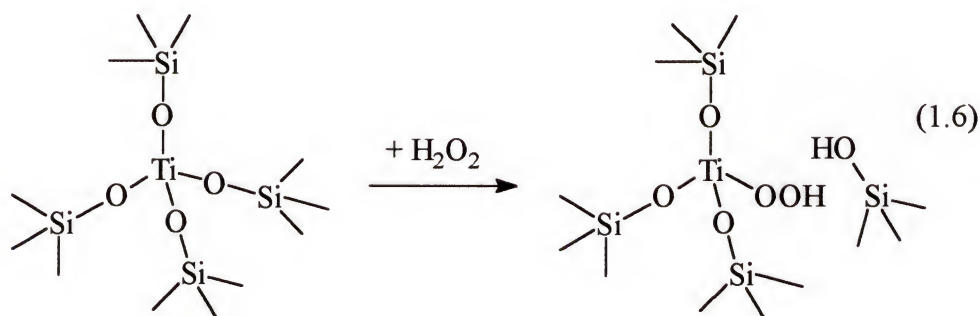


The active species is the inorganic analog of the species proposed in the reaction between hydrogen peroxide and activated ketones such as hexafluoroacetone. The use of aqueous hydrogen peroxide introduces certain problems in the system, as compared to the use of organic hydroperoxides. A polar solvent, such as an alcohol or ether is required to dissolve both H_2O_2 and olefin. These solvents and the water present compete for coordination to the metal, reducing the epoxidation rates. Metals are affected by the presence of water to different extents, following the order $\text{W} < \text{Mo} < \text{Ti} < \text{V}$. Some of the highest selectivities were obtained by the use of NaHWO_4 in basic solution.

Venturello et al. reported in 1983 that sodium tungstate in the presence of phosphoric acid and a phase transfer catalyst was able to catalyze the epoxidation of terminal olefins with diluted H_2O_2 (8%) in biphasic conditions.³⁶ A similar biphasic method was found by Ishii and co-workers, who reported that a heteropolyacid containing tungsten catalyzes the epoxidation using 35 % H_2O_2 , leading to an increase in the yield of epoxide.³⁷ Both systems^{36,37} required chlorinated solvents such as dichloromethane or chloroform in order to obtain good results. Recently new systems have been developed which do not require environmentally unfriendly chlorinated solvents. The reactions can be performed in the absence of solvents or with added toluene. Sodium tungstate, aminomethylphosphonic acid and methyltrioctylammonium hydrogensulfate perform the epoxidation of unactivated olefins with aqueous hydrogen peroxide (30 %) with high selectivity and conversions.³⁸ The nature of the phase transfer catalyst and the phosphonic acid derivative were very important in the reaction. Another approach to the problem of mixing between the organic aqueous phases was developed by Newmann and Miller.³⁹ A phase transfer catalyst, a quaternary ammonium salt, was incorporated on the

surface of a silica particle. This positively charged species brings both the anionic tungstate species and the olefin together on the silica surface, where oxidation can take place.

Recently a heterogeneous system was found that can activate hydrogen peroxide for a series of oxidations, including the epoxidation of small olefins.⁴⁰ Titanium silicalite (TS-1) is a zeolite with a structure similar to ZSM-5 where a small percentage of titanium is isomorphously incorporated in the framework replacing silicon atoms.⁴¹ There is a limit to the amount of titanium that can be incorporated in the structure, and attempts to incorporate more than 3 % Ti lead to titania nanophases.⁴² A variety of substrates including alcohols, ketones, alkanes and alkenes can be selectively oxidized with minimal hydrogen peroxide decomposition. Titanium centers inside the zeolite channels are assigned as the active species since silicalite-1, an isomorphous material with no titanium, is inactive for oxidation. Dispersion of the titanium at the atomic level is crucial to avoid Ti-O-Ti bonds. The hydrolysis of the Ti-O-Si bond by peroxide is believed to generate the active species.



Surprisingly, TS-1 is unaffected by the presence of water in the reaction mixture. Dilute aqueous solutions of hydrogen peroxide can be used with no reduction in activity or

selectivity. As a comparison, when an amorphous, coprecipitated titania-silica catalyst is used with aqueous H_2O_2 , no reaction is observed.⁴³ Part of the distinct behavior of TS-1 can be explained by the hydrophobic nature of the internal channels. Drago and co-workers⁴⁴ recently studied the properties of the TS-1 surface. The Cal-Ad method (a method combining calorimetric and adsorption measurements to define the acid sites in a solid) and the Multiple Equilibrium Analysis (MEA) identified a very low number of hydrogen bonding sites (as compared to ZSM-5 and silica gel) and no strong acid sites. The absence of a large number of hydrogen bonding sites (Si-OH groups) is believed to be the cause of TS-1's hydrophobicity. The catalyst is able to preferentially absorb the hydrocarbon substrate and thus water cannot compete for the active sites with hydrogen peroxide. On the other hand, no epoxidation is observed when t-butyl hydroperoxide is used as the oxidant, apparently due to size constraints inside the pores. When titanium is dispersed on silica, the reverse is observed: Aqueous H_2O_2 does not lead to oxidation and very good yields were reported with the organic hydroperoxide. In a very recent article, however, a catalyst prepared by the dispersion of TiF_4 on silica was shown to perform the epoxidation of cyclohexene with concentrated hydrogen peroxide (70 %).⁴⁵ Yields and selectivities were much better when an organic hydroperoxide was used. Increasing the amount of water in the reaction by using 30 % H_2O_2 led to very low conversion but adding the hydrogen peroxide in small portions led to much higher yields when compared to a one time addition. These results indicate that the hydrophilic nature of silica limits its use as a support for titanium when hydrogen peroxide is the oxidant. One advantage in the use of silica is that it does not present the size constraints of the zeolitic materials like TS-1, so larger substrates can be oxidized.

Sharpless and collaborators^{46,47} recently found that the epoxidation of olefins by H_2O_2 catalyzed by methyl trioxorhenium (MTO) can be accelerated by the addition of an excess of substituted pyridines. An unusually high activity was observed for the epoxidation of unactivated terminal olefins. In the absence of excess pyridine, the rate is lower and the yields are poor for those olefins, intimating that pyridine has a dual role of Ligand Accelerated Catalysis (LAC) and base. The presence of the base reduces the Lewis acidity of the medium and thus protects the epoxide.

Complexes of iron with macrocyclic ligands such as cyclam (1,4,8,11-tetraazacyclotetradecane) have been found⁴⁸ to catalyze the epoxidation of olefins with aqueous hydrogen peroxide in acetonitrile, but no epoxide was found when other metal ions were used (Mn(II), Co(II), Ni(II) and Cu(II)). These systems presented unusual peroxide selectivities and low amounts of allylic oxidation products. The epoxidation might require coordination of a HOO^- to the iron center. No epoxide was observed when organic hydroperoxides were used as the oxidants.

Alkyl Hydroperoxides

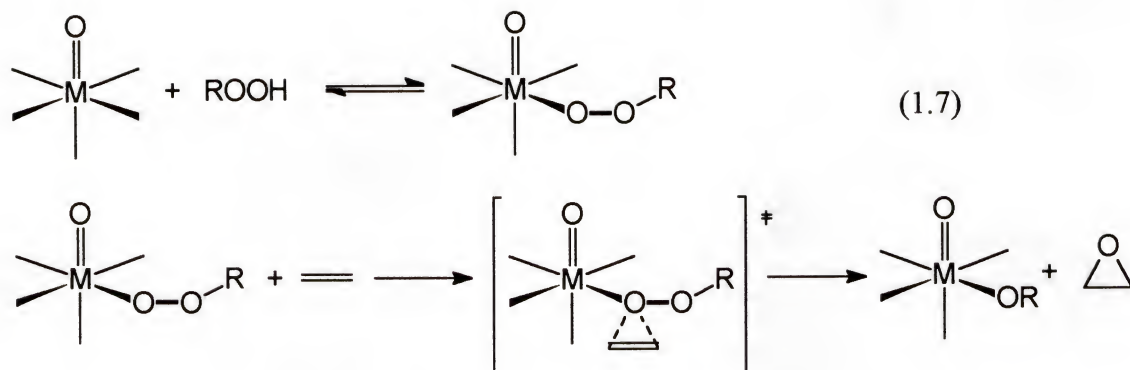
Alkyl hydroperoxides are generated by the autoxidation of hydrocarbons. Examples of alkyl hydroperoxides used in oxidations include t-butyl hydroperoxide (TBHP), cyclohexyl hydroperoxide (CHP), ethyl benzyl hydroperoxide (EBHP) and cumene hydroperoxide. Utilizing a homogeneous molybdenum catalyst in conjunction with an alkyl hydroperoxide, the ARCO process for the epoxidation of propene is responsible for the production of more than one million tons of propylene oxide annually.⁴⁹ When using an organic hydroperoxide, the alcohol generated as the co-

product must be recycled or sold, which is an economic limitation of the process.⁵⁰ If the process uses TBHP, the t-butyl alcohol generated can be sold or converted to methyl t-butyl ether, a gasoline octane booster. In the case of ethylbenzyl hydroperoxide, the corresponding alcohol is dehydrated to styrene, a valuable commodity. TBHP is much more stable than H_2O_2 , both with respect to thermal decomposition (the half life of dilute solutions of TBHP in benzene is 520 hours at 130°C) and to metal contaminants. In the absence of metal catalysts, TBHP is unreactive toward most organic compounds, including olefins.⁵¹ The greater stability of organic peroxides and the price of hydrogen peroxide are some of the factors favoring this technology in industry.

Homogeneous catalysts used in combination with organic hydroperoxides generally exhibit the following characteristics:⁵²

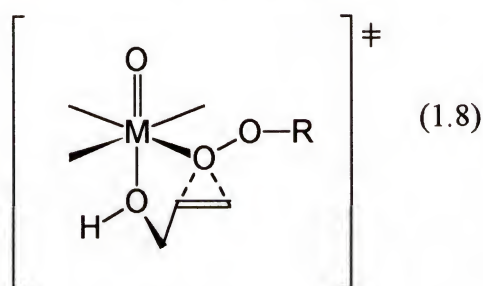
- (1) metals which are strong Lewis acids in their highest oxidation states are generally excellent catalysts. These include, in order of activity, $\text{Mo} > \text{W} > \text{Ti}, \text{V}$. First row transition metals decompose the peroxides and are not catalysts.
- (2) polar solvents, such as alcohols and water decrease the reaction rate by competing with peroxides for the active sites of the catalyst. Since the use of an alkyl hydroperoxide generates alcohols, this by-product affects rate as the reaction proceeds.
- (3) indicative of the electrophilic nature of the active oxidant species, electron donating groups in the olefin increase the reaction rate.

The epoxidation of olefins using these transition metal catalysts and alkyl hydroperoxides has been suggested to involve the formation of a hydroperoxide complex which is similar to the proposed mechanism for hydrogen peroxide:



Work by Sheldon on the mechanism of molybdenum catalyzed epoxidation of olefins with alkyl hydroperoxides⁵³ has suggested that two competing processes are catalyzed by the metal: epoxidation of the olefin and hydroperoxide decomposition.

In the epoxidation of allylic alcohols, coordination of the alcohol to the metal center appears to induce high stereoselectivity for the reaction:



Sharpless and Katsuki⁵⁴ have successfully exploited this interaction for the asymmetric epoxidation of olefins, using titanium isopropoxide and a chiral di-ethyl tartrate. The process only works with allylic alcohols and initially used a stoichiometric amount of titanium. Recently a modified procedure has led to a real catalytic process.⁵⁵ Enantiomeric excesses for the systems described were between 84 and 98 %.

A commercial process assigned to Shell Oil Company utilizes t-butyl hydroperoxide or ethylbenzene hydroperoxide together with 2% titanium supported on silica. The titanium is added as TiCl_4 and the solid is then calcined. Conversions of propylene to propylene oxide are greater than 97 %, with selectivities around 90 %. Other systems have been described attempting to obtain a better dispersion of the titanium on the surface. Silica gel has been treated with titanium isopropoxide, producing a catalyst able to epoxidize olefins with t-butyl hydroperoxide.⁵⁶ When silica is used as a support, silylation of acidic groups present on the surface greatly increases selectivities for the epoxidation reaction.⁵⁷ One of these systems uses a molybdenum oxide or a mixture of titanium and molybdenum oxides dispersed on silica.⁵⁸ These processes are comparable to the use of TS-1 as an epoxidation catalyst.

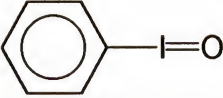
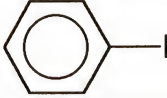
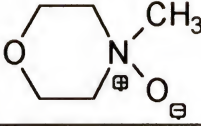
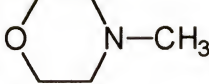
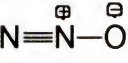
Examples of the use of heterogeneous catalysts include recent work⁵⁹ patented by Arco Chemical and utilizes transition metal compounds supported in a porous carbon molecular sieve. Molybdenum, titanium, chromium and vanadium have all been used in this way and an organic hydroperoxide functions as the oxidant.

Chromium silicalite is also capable of using a hydroperoxide as oxidant.⁶⁰ This material is a redox zeolite, in which chromium is incorporated to the silicon/aluminum framework. Controversy remains on whether the metal is actually incorporated in the framework of the solid.

Other Oxidants

Many other oxygen transfer reagents have been used for the epoxidations of olefins and will be described here. These reagents are listed on Table 1.1.

Table 1.1. Oxygen atom transfer reagents and active oxygen percentages

Reagent	Structure	Co-product	Active Oxygen (%)
Iodosylbenzene			7.27
Sodium periodate	NaIO ₄	NaIO ₃	7.48
N-methylmorpholine N-oxide (NMO)			13.6
Sodium hypochlorite	NaOCl	NaCl	21.49
Nitrous oxide		N ₂	36.35

There are several important features related to the choice of the oxidant. The percentage of active oxygen should be as high as possible. The price and availability are obvious aspects, as well as the toxicity and environmental impact of the reagent. Another important condition for the success of an oxidant is the choice of solvent. The use of chlorinated solvents (which normally give very good results for epoxidation) should be avoided, since this contradicts the utility of using an environmentally friendly oxidant.

Iodosylbenzene (PhIO) is prepared by the hydrolysis of the corresponding diacetate with NaOH. Even though iodosylbenzene is a very expensive and toxic material, it has been used in a large number of studies due to its high activity and selectivity. Many coordinatively unsaturated salts of transition metals such as the triflate salts of Mn(II), Fe(II), Co(II) and Cu(II), are active catalysts for oxidations by iodosylbenzene.⁶¹ Mn (III) salen (salen= N, N'-ethylenebis(salicyledeneaminato)) complexes are also

catalysts for the epoxidation of olefins in the presence of PhIO.⁶² The activity of the catalysts could be modulated by placing different substituents in the aromatic ring of the salen ligand and electron withdrawing groups were found to enhance the activity of the catalyst. The chromium complexes using the same ligand system were also studied and showed lower activity. The oxochromium (V) intermediate was isolated and characterized by X-Ray crystallography.

Kochi's work paved the way for the development of a very important process for the asymmetric epoxidation of olefins. Jacobsen synthesized a Mn(III) salen derivative from the condensation of a substituted salicylaldehyde and a chiral diamine, generating a very sterically hindered, rigid catalyst. The ligands direct the approach of the olefin to the Mn^VO , in such a way that one of the enantiomers was produced preferentially. The catalyst can utilize NaOCl as the oxidant, in a biphasic system containing a phase-transfer catalyst (PTC). Other asymmetric epoxidation systems have been developed using chiral porphyrins in conjunction with iodosylbenzene.^{63, 64, 65}

The use of NaOCl in similar conditions (biphasic system with PTC) was also studied in the case of Ni(II) complexes of salen⁶⁶ and cyclam. NaOCl, in the form of the commercial aqueous bleach solution (0.77 M) is an inexpensive oxidant. The use of NaOCl leaves NaCl as waste and can form very toxic chlorinated by-products.

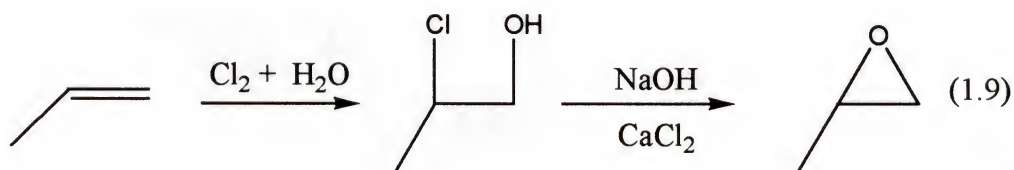
Sodium periodate and NMO have been used as oxidants with a variety of ruthenium catalysts.⁶⁷ Sodium periodate leaves an equimolar amount of sodium iodate as waste, and NMO is a very expensive oxidant.

N_2O is a co-product in the oxidation of cyclohexanol and cyclohexanone to adipic acid by nitric acid. Very large amounts of this gas are produced and it is considered an

important environmental problem. A process has been developed to use N_2O in the hydroxylation of benzene to phenol, catalyzed by iron/ZSM-5. Groves has found that a ruthenium porphyrin is able to epoxidize olefins using N_2O as the oxidant.⁶⁸

Hindered olefins react with nitric oxide producing epoxides.⁶⁹ The reaction is catalytic when O_2 is present, with NO being re-oxidized to NO_2 . The reaction is only selective to the epoxide when the double bond is surrounded by bulky substituents.

The epoxidation of propylene can be performed without the use of an oxygen atom transfer reagent such as those mentioned so far. In the chlorohydrin process commercialized by Dow Chemical and still in use in some places, chlorine gas is the oxidant. The intermediate chlorohydrin is hydrolyzed in the presence of base and $CaCl_2$.



Conclusions

The epoxidation of olefins continues to be of major interest inside the chemical oxidations field, as evidenced by the large number of recent publications. The reaction has been studied due to its practical importance, its biological relevance and the fundamental knowledge that can be obtained. A large number of organic reagents and a larger yet number of transition metal containing compounds combined with a variety of oxidants has been used in the synthesis of epoxides. The intricacies of the reaction and the variety of

methods and mechanisms, coupled with challenges like the asymmetric epoxidation, will keep this area intensely researched in the years to come.

CHAPTER 2

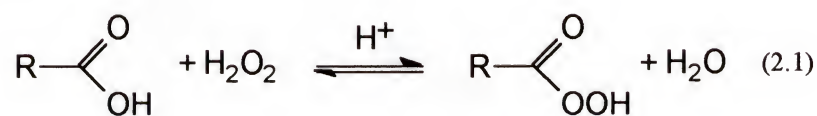
THE EPOXIDATION OF OLEFINS USING PEROXY ACIDS GENERATED *IN SITU*

Introduction

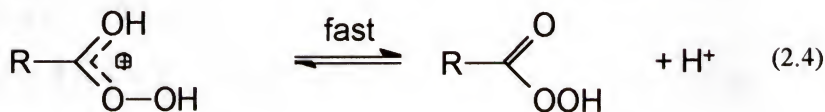
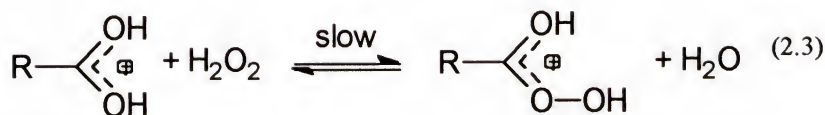
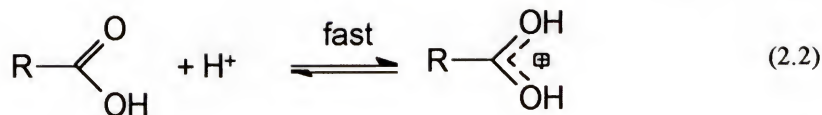
The formation of peroxy acids from hydrogen peroxide and carboxylic acids is the single major industrial use of hydrogen peroxide.³² Peroxyacetic acid formed *in situ* from acetic acid and H₂O₂ is used in the preparation of Epoxidized Soya Bean Oil (ESBO), which is then used as a plasticizer/stabilizer for polyvinyl chloride.³² Peracids are also used in the oxidation of several other compounds and as a chlorine alternative in the paper bleaching industry.⁷⁰ These examples show the importance of the peracid route for hydrogen peroxide activation.

The Formation of Peracids

Peracids can be formed in several different ways. Of particular interest to this work is the reaction of a carboxylic acid and hydrogen peroxide, equation (2.1):

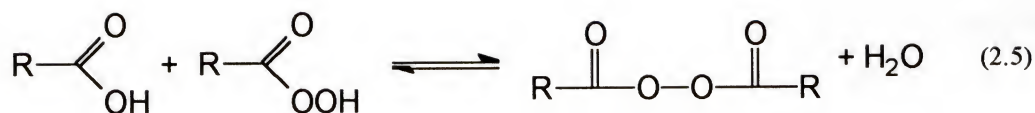


The equilibrium in (2.1) is very slowly achieved in the absence of an acid catalyst.⁷¹ A mechanism for the acid-catalyzed peracid formation similar to that of esterification reactions has been proposed (equations 2.2-2.4).⁷²

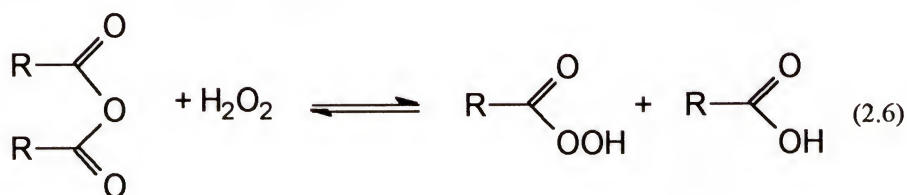


Acid catalysts used in industry include sulfuric acid, phosphoric acid and Amberlyst 15®, an ion-exchange resin in the acid form.⁷² The concentration of sulfuric acid has been shown to affect both the rate of formation and the final equilibrium amount in the case of peracetic acid. It is believed that the acid removes water, displacing the equilibrium in equation 2.3 to increase the formation of peroxy acid. For the preparation of aromatic peracids such as perbenzoic acid, methanesulphonic acid is used. When a very strong carboxylic acid is employed like trifluoroacetic or formic acid, no acid catalyst is necessary.⁷³ Many applications, including the epoxidation of olefins, require the peracid to be acid free due to the acid-sensitive nature of the product. Acid removal can be accomplished by distillation or extraction of the peracid, or by neutralization of the remaining free acid. It is preferable however to generate and use the peracid *in situ*, thus avoiding the dangerous and costly steps of separation and storage.

A large excess of carboxylic acid should be avoided, since the peroxy acid can react with the excess acid forming explosive dialkyl peroxides (equation 2.5):⁷²



As seen in equation (2.1), the removal of water displaces the equilibrium towards the production of peracid. Carboxylic acid anhydrides can also be used to generate peracids (2.6):



When the anhydride is used, a water-free peracid solution is generated and higher concentrations of peracid can be obtained.

The formation of peracid-like species from hydrogen peroxide is not restricted to carboxylic acids. Other reagents that are able to undergo perhydrolysis with hydrogen peroxide are listed in Table 2.1.⁷¹⁻⁸² As with peroxycarboxylic acids, a conjugated double bond is common to most of these compounds and is postulated to activate the peroxide moiety.

Several of the species in Table 2.1 were only postulated in the literature, and have not been isolated. Many of these are claimed to be useful substitutes to meta-chloroperbenzoic acid, MCPBA. Due to the hazards associated with the manufacture, storage and shipping of strong oxidizers, an *in situ* generated peracid-like substitute

Table 2.1. Formation of peroxy acid-like species by reaction with hydrogen peroxide and co-products after oxidation

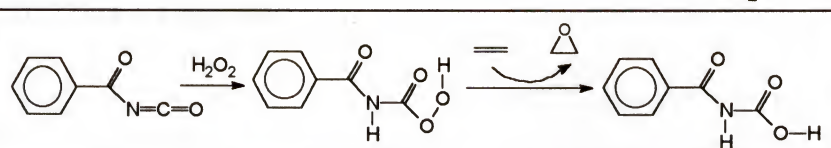
Reagent	Peracid Formation / Olefin Epoxidation
Nitriles ⁷⁴	$\text{R}-\text{C}\equiv\text{N} \xrightarrow{\text{H}_2\text{O}_2} \text{R}-\text{C}(\text{N}=\text{H})\text{OOH} \xrightarrow{\text{epoxide}} \text{R}-\text{C}(=\text{O})\text{NH}_2$
Acid Chlorides ⁷¹	$\text{R}-\text{C}(=\text{O})\text{Cl} + \text{OOH}^- \longrightarrow \text{R}-\text{C}(=\text{O})\text{OOH} + \text{Cl}^- \xrightarrow{\text{epoxide}} \text{R}-\text{C}(=\text{O})\text{OH}$
Ketones ^{75,76}	$\text{R}_1-\text{C}(=\text{O})-\text{R}_2 \xrightarrow{\text{H}_2\text{O}_2} \text{R}_1-\text{C}(\text{OOH})(\text{OH})-\text{R}_2 \xrightarrow{\text{epoxide}} \text{R}_1-\text{C}(\text{OH})_2-\text{R}_2$
Cyanoformates ⁷⁷	$\text{R}-\text{O}-\text{C}(=\text{O})\text{CN} \xrightarrow{\text{H}_2\text{O}_2} \text{R}-\text{O}-\text{C}(=\text{O})\text{OOH} + \text{HCN} \xrightarrow{\text{epoxide}} \text{R}-\text{O}-\text{H} + \text{CO}_2$
Chloroformates ⁷⁸	$\text{R}-\text{O}-\text{C}(=\text{O})\text{Cl} \xrightarrow{\text{H}_2\text{O}_2} \text{R}-\text{O}-\text{C}(=\text{O})\text{OOH} + \text{HCl} \xrightarrow{\text{epoxide}} \text{R}-\text{O}-\text{H} + \text{CO}_2$
Isocyanates ⁷⁹	$2 \text{R}-\text{N}=\text{C}=\text{O} \xrightarrow{\text{H}_2\text{O}_2} \text{R}-\text{N}(\text{H})-\text{C}(=\text{O})\text{OOH} \xrightarrow{\text{epoxide}} \text{R}-\text{N}(\text{H})-\text{C}(=\text{O})-\text{N}(\text{H})-\text{R} + \text{CO}_2$
Benzoyl isocyanate ⁸⁰	
Cyanates ⁸⁰	$\text{R}-\text{O}-\text{C}\equiv\text{N} \xrightarrow{\text{H}_2\text{O}_2} \text{R}-\text{O}-\text{C}(\text{N}=\text{H})\text{OOH} \xrightarrow{\text{epoxide}} \text{R}-\text{O}-\text{C}(=\text{O})\text{N}(\text{H})_2$

Table 2.1. (continued)

Reagent	Peracid Formation / Olefin Epoxidation
Carbonyldi triazole ⁸⁰	
Carbodiimides ^{80,81}	
Ethyl orthocarbonate ⁷⁶	
Hydrogen carbonate anion ⁸²	

is proposed. Another reason for seeking a substitute to MCPBA is in the preparation of acid-sensitive epoxides, where MCPBA and other related peracids can lead to low yields. Unfortunately, most of these replacements are stoichiometric in nature. Once the peracid concentration is depleted, the co-product is difficult to regenerate to its dehydrated form.

Nitriles have been shown⁷⁴ to react with hydrogen peroxide in alkaline solution to form peroxyimidic acids, which are able to perform epoxidations. The neutral amide product makes this a system suitable for the epoxidation of acid-sensitive epoxides. Peroxyimidic acids have not been isolated. The peroxyimidic acid is supposed to decompose by reaction with the perhydroxyl ion (2.7), a reaction that competes with epoxidation.



Examples of nitriles used include acetonitrile, chloroacetonitrile and benzonitrile.

Hexafluoropropylene oxide is prepared in large scale by this method.⁸³

Activated ketones such as hexafluoroacetone⁷⁵ and tetrachloroacetone⁷⁶ can react with hydrogen peroxide forming peroxyacids. Hexafluoroacetone generates a very strong oxidizing system, being able to perform the conversion of ketones to esters (Baeyer-Villiger reaction). In the case of tetrachloroacetone, epoxides can be obtained only if a solid buffer such as Na_2HPO_4 is added to the mixture, since the co-product geminal diol is very acidic. The geminal diol is thermally unstable, returning to the initial ketone with heat. The system can be made catalytic by refluxing the mixture and continuously distilling water out as an azeotrope.

Peroxycarbonic acids can be generated by the reaction of cyano⁷⁷ and chloroformates⁷⁸ with hydrogen peroxide. Reactions involving chloroformate were run under biphasic conditions. Aqueous hydrogen peroxide (30 %) containing a buffer and CH_2Cl_2 containing chloroformate and olefin were reacted. Percarbonic acid formation occurs at the interface, accompanied by a drop in the pH due to HCl formation. In the case of cyanoformates, the reaction was run either in CH_3CN or CH_2Cl_2 and the weak acid HCN released dispensed with the need for a buffer to avoid ring opening. Chiral cyanoformates were also prepared and led to small enantiomeric excesses (20 % maximum).

Peroxycarbamic acids are formed by the reaction of isocyanates and hydrogen peroxide. When phenyl isocyanate⁷⁹ and hydrogen peroxide are mixed in the presence of

an olefin, epoxidation occurs and 1,3-diphenylurea and carbon dioxide are formed as co-products. The use of p-chlorophenyl isocyanate increased the epoxide yields as did the use of non-polar solvents such as benzene or n-pentane. Benzoylperoxycarbamic acid⁸⁰ (BPC) can be formed by reaction of benzoyl isocyanate and hydrogen peroxide and can be used for epoxidation. BPC has been isolated and can also be used in its crystalline form.⁸⁴

Aryl cyanates bound to a polymer were reacted with H_2O_2 and the intermediate percarbamic acid was able to produce epoxides from olefins, although in very low yields.⁸⁰ The carbamate co-product was hydrolyzed back to the phenol and could in theory be recycled to the cyanate by reaction with BrCN . Even though the polymer made separation of reactant and products easy, the yields were too low to make the process useful.

Carbodiimides⁸⁰ are another example of a reagent able to undergo reaction with hydrogen peroxide, producing an intermediate peracid similar to that produced by the reaction of nitriles and H_2O_2 . This system has been used successfully in the synthesis of arene oxides, which are very sensitive to acids, high temperature or hydroxylic solvents.⁸¹

Carbonylditriazole (CDT)⁸⁰ was reacted with H_2O_2 and substituted olefins in THF, producing epoxides in 98-99 % yield. The reaction rates were independent of the solvent basicity, which is generally opposite to that found in conventional peracids. This could indicate that the intramolecular hydrogen bond in the intermediate peracid for the CDT system is not as easily disrupted as in peroxycarboxylic acid systems.

Ethyl orthocarbonate⁸⁰ was also able to produce epoxides from olefins in the presence of hydrogen peroxide. In this case, as in the case of the activated ketones, there is no double bond for the internal hydrogen bond. In the postulated structure the hydrogen from the perhydroxyl group is bonded to one of the ethoxy groups. These

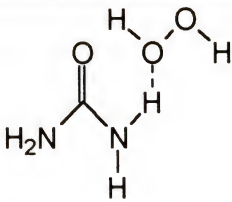
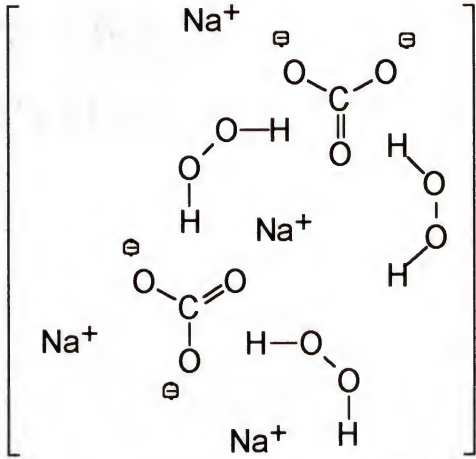
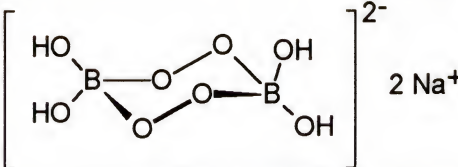
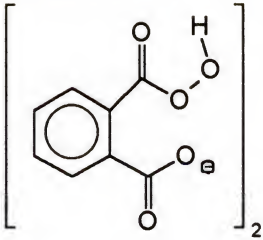
examples show that the π bond present in peroxy-carboxylic acids and many of the examples shown above is not necessary for oxygen transfer.

The perhydrolysis of imidazolidines⁸⁵ and of acyl dialkyl phosphates⁸⁶ can be useful to generate peroxy acids containing electron-donating substituents like p-methoxyperbenzoic acid, where the direct reaction between the carboxylic acid and hydrogen peroxide does not proceed to a large extent.

The presence of water in the reaction mixture affects the formation of peracids in an adverse manner, reducing conversion of the carboxylic acid significantly. For instance, if a mixture containing 98 % hydrogen peroxide, an equivalent amount of acetic acid and 1 % sulfuric acid is allowed to reach equilibrium to form peracetic acid, a solution of around 50 % peracid is formed. This can be compared to yields of 40% peracid when using 90 % H_2O_2 and only 10 % conversion to peracid when 30 % H_2O_2 is used.⁷² The use of hydrogen-bonded adducts as the source of anhydrous hydrogen peroxide has received attention. These adducts can be used as a replacement to highly concentrated peroxide solutions. Table 2.2 lists some of these adducts and their respective percentage of active oxygen by mass. As a comparison, anhydrous hydrogen peroxide has 47 % active oxygen (1 oxygen atom in H_2O_2).

The urea-hydrogen peroxide adduct (UHP) is a very good source of neutral, anhydrous H_2O_2 , and is limited only by its solubility in organic solvents.⁸⁷ Sodium percarbonate (SPC) is another commonly used source. Commercial sodium percarbonate is simply a hydrogen-bonded adduct formed by the crystallization of hydrogen peroxide solutions containing sodium carbonate. SPC has very limited solubility in organic

Table 2.2 - Hydrogen peroxide adducts and other solid oxidants

Name	Formula / structure	% Active oxygen
Urea Hydrogen Peroxide (UHP) ⁸⁷		17.0
Sodium Percarbonate (SPC) ⁸⁸⁻⁹⁰	$\text{Na}_2\text{CO}_3 \cdot 1\frac{1}{2}\text{H}_2\text{O}_2$ 	15.3
Sodium Perborate (SPB) ^{89,90}		20.8
Triphenyl phosphine oxide adduct ⁹¹	$\text{Ph}_3\text{PO} \cdot \frac{1}{2} \text{H}_2\text{O}_2$	2.7
Magnesium monoperoxy phthalate (MMPP) ⁹¹	 $\text{Mg}^{2+} \cdot 6 \text{H}_2\text{O}$	6.5
Oxone ⁹²	$(\text{KHSO}_5)_2 \cdot \text{KHSO}_4 \cdot \text{K}_2\text{SO}_4$	5.2

solvents, releasing its peroxide very slowly in the absence of water. Ultrasound techniques have been used to improve dissolution.⁸⁸ SPC has been used for epoxidations together with peracid precursors such as carboxylic acids and nitriles.⁸⁹ SPC is moisture sensitive, with the peroxide decomposing quickly in water.

Another important source of anhydrous hydrogen peroxide is sodium perborate (SPB).⁸⁹ Unlike the UHP and SPC, sodium perborate is not an adduct, but presents the cyclic formula shown in Table 2.2. It has also been used in a very diverse number of oxidations, including epoxidations, in many cases through the formation of peracids.⁹⁰ The use of adducts such as UHP, SPC and SPB becomes especially important when synthesizing acid-sensitive epoxides, where the presence of water can lead to the formation of diols.

Magnesium monoperoxyphthalate hexahydrate (MMPP) is a stable solid compound that can be used for epoxidations. For the epoxidation to proceed it has to be dissolved in a polar solvent such as a low molecular weight alcohol or a phase transfer catalyst should be used to carry the anion to the organic phase containing the olefin.⁹¹

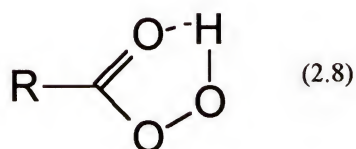
Oxone® is the commercial name of a solid mixture of potassium salts of hydrogen persulfate, hydrogen sulfate and sulfate. It is a very strong oxidizing agent and has been used for the oxidation of sulfides such as mustard gas ($S(CH_2CH_2Cl)_2$).⁹²

The formation of peroxyacids can be catalyzed by enzymes. Lipases were used to catalyze the reaction of hydrogen peroxide and carboxylic acids, forming peroxycarboxylic acids *in situ* which then performed epoxidations.⁹³ The process is considered a milder alternative to the acid catalyzed synthesis of peroxyacids where the presence of acid can lead to ring opening of the epoxide.

Carboxylic acid-type ion exchange resins have been used to generate heterogeneized peracids by reaction with hydrogen peroxide in acid solution.⁹⁴

Characteristics of Peracids

In non-coordinating solvents, such as carbon tetrachloride, peroxy acids exist in a monomeric structure presenting a intramolecular hydrogen bond (2.8). This contrasts with the behavior of carboxylic acids where polymeric forms are more stable. This very stable hydrogen bond is responsible for several of the differences in the physical characteristics of peracids when compared to their parent acids. The boiling points of peracids, for instance, are lower than those of the related carboxylic acids, even though they have a higher molecular weight (one extra oxygen atom). This is explained by the stability of the intramolecular bond, in contrast to the intermolecular bond in carboxylic acids.



The intramolecular hydrogen bond is disrupted in basic solvents (2.9). The interactions between several bases and peroxybenzoic acids have been quantified using calorimetric and NMR techniques.⁹⁵



Reaction enthalpies for the interaction of peracids and bases and the shifts for the H^1 NMR of the OOH peak (as compared to the values in CCl_4) were found to be linear and dependent on the acidity of the peroxy acid as well as the basicity of the oxygen donor base.⁹⁵ A crystalline, stable adduct between p-nitroperbenzoic acid and triphenylphosphine oxide has been isolated and its structure determined by X-ray crystallography.⁹⁶

The acidity of peracids is considerably weaker than that of the parent carboxylic acid. This weakening occurs because of the reduction of the inductive effect by the introduction of a second oxygen between the acyl group and the proton.⁷¹

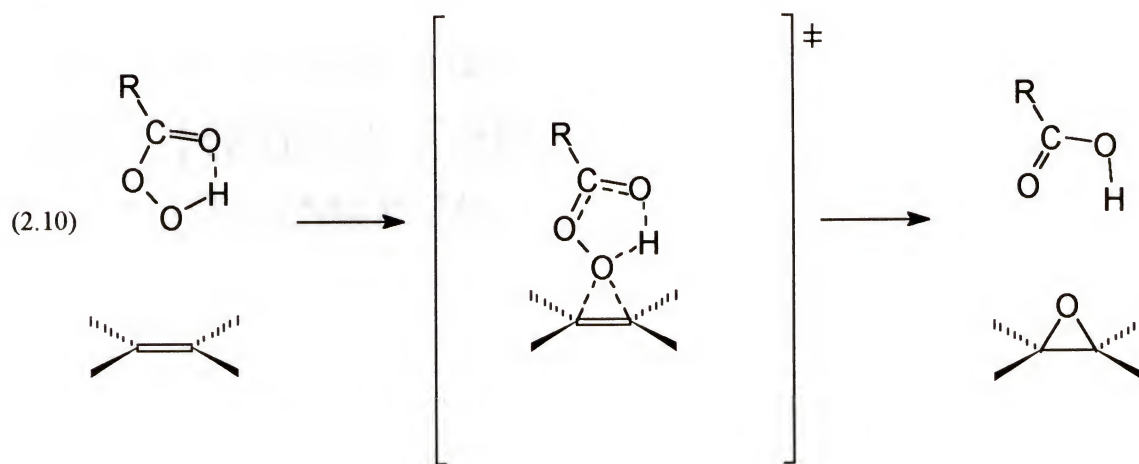
Mechanism of the Epoxidation of Olefins by Peracids

The reaction of peroxy acids with olefins to form epoxides was discovered almost one hundred years ago and is known as the Prilezhaev reaction.⁹⁷ Experimental evidence points toward electrophilic attack by the peracid on the olefin. Some characteristics of this reaction are listed below:

- the reaction is second order;
- rates are increased by electron withdrawing groups on the peracids or by the presence of electron donating groups on the olefins. The reaction has calculated Hammett ρ values of +1.4 for substituted perbenzoic acids and -1.3 for substituted aromatic olefins;⁹⁸
- the oxygen atom transfer is stereospecific, with cis-alkenes producing only cis-epoxides and trans alkenes producing only trans epoxides;

- the reaction is not influenced by steric effects;
- the reaction has a strong solvent effect, being slowed by hydrogen bonding, basic solvents.

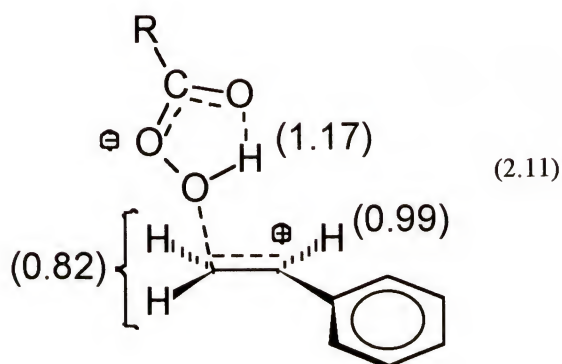
These results led to the proposition of the "butterfly" transition state by Bartlett⁹⁹ in 1957. In the proposed transition state, oxygen is transferred in a concerted step from the intermolecularly bonded peracid. The symmetrical, planar transition state is shown in (2.10):



The experimental evidence is well accommodated by this mechanism. The electronic effects are explained by considering the oxygen being transferred as electrophilic. Electron withdrawing groups on a peracid increase its electrophilicity. Electron donating groups on the olefin will increase its reactivity towards the electrophile. The concerted mechanism explains the stereospecificity of the reaction, eliminating the possibility of rotation along the double bond. It can be seen in the scheme above that steric effects would not be expected in this mechanism. Finally, the drastic reduction in rates in the

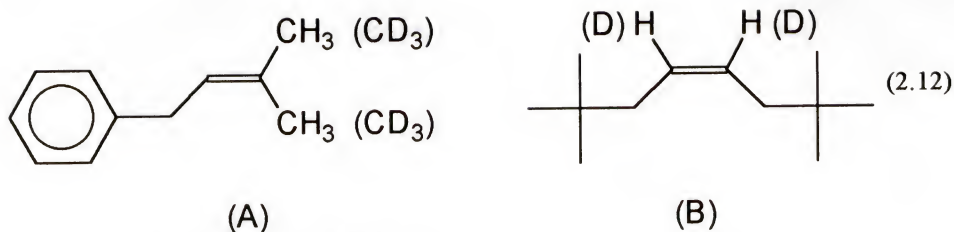
presence of basic solvents is explained by the disruption of the intramolecular hydrogen bond which is necessary for concerted oxygen transfer (equation 2.9).

Although this model is still very popular, there is some controversy in the literature about the mechanism for the epoxidation of olefins with peracids. One of the most solid criticisms of the model came from kinetic isotope effect experiments by Hanzlik and Shearer. The reaction rate ratios (k_H/k_D) for the epoxidation of substituted styrenes with meta-chloroperoxybenzoic acid are shown in parentheses next to the corresponding hydrogens in (2.11).¹⁰⁰



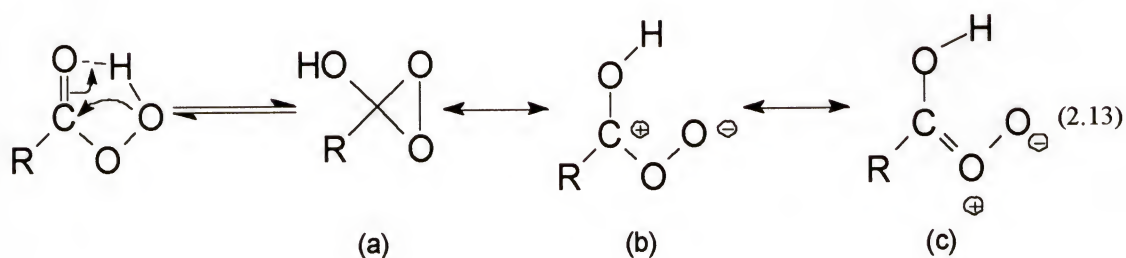
Since the hydrogens in the $=CH_2$ portion of the olefin gave rise to a significant inverse isotope effect ($k_H/k_D = 0.82$), and the hydrogen in the $=HAr$ portion did not ($k_H/k_D = 0.99$), it was concluded that the transition state had to be unsymmetrical, with large charge separation and an open configuration, as shown in (2.11). Theoretical studies using *ab initio* calculations found the transition state to be unsymmetrical with one of the double bonded carbons presenting sp^3 character due to the C-O bond formation, while the other retained sp^2 hybridization, corroborating Hanzlik's transition state.¹⁰¹

A more recent work¹⁰² revisited the kinetic isotope effect discussion by measuring the α and β secondary isotope effects in the olefins shown below (2.12):



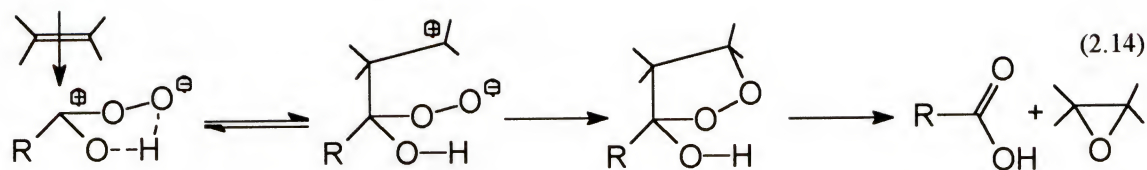
The results for both the β isotope effect (from (A)) and from the symmetrical olefin (B) indicate that the transition state is symmetrical. The differences seen by Hanzlic are thought to come from differences in electron density on an unsymmetric olefin. These results support Bartlett's concerted mechanism.

Other mechanisms involving charge separation have been proposed. Kwart proposed that peracids can go through a pericyclic rearrangement to form a hydroxy dioxirane (2.13a). The canonical forms (2.13b) and (2.13c) of the dioxirane would present a 1,3 or 1,2 charge separation.

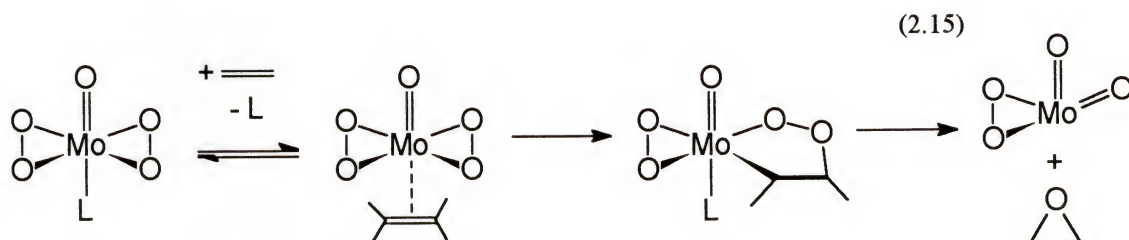


Kwart and Hoffman proposed an epoxidation mechanism, with a 1,3 charge separation on the peracid (11b).¹⁰³ This mechanism was later discarded by the large differences in the effect of substituents and in entropy of activation between epoxidation and 1,3-dipolar additions.¹⁰⁴

Mimoun proposed an alternative mechanism by modifying Kwart and Hoffman's 1,3-dipolar mechanism (2.14).⁹⁶



The first step in this mechanism involves the formation of a charge-transfer π complex between the nucleophilic olefin and the electrophilic carbon atom derived from the 1,3 charge separation. Such olefin complexes were proposed in the mechanism of the reaction between MoO_3L and alkenes (2.15).

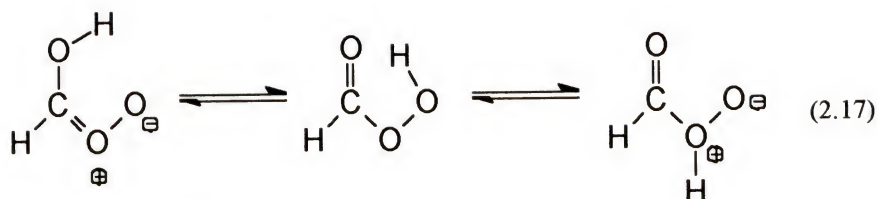


After the olefin is coordinated, nucleophilic attack of the terminal oxygen on the olefin takes place. The author suggests that after complexation the olefin loses its nucleophilicity, thus allowing for the attack of the negatively charged oxygen atom.

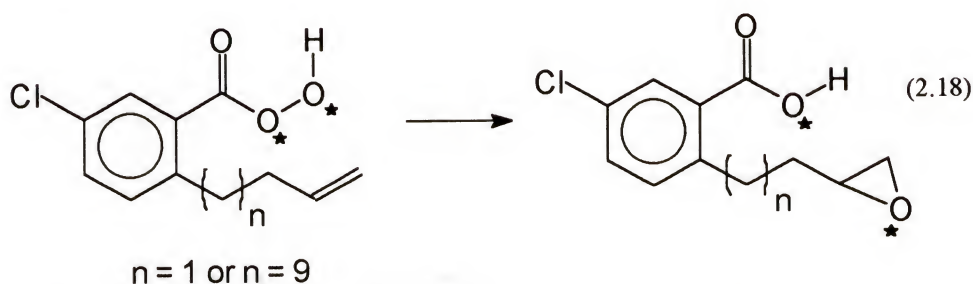
Bach and co-workers¹⁰⁵ performed *ab initio* theoretical studies on the transition state of the epoxidation of ethylene by performic acid. He investigated if the epoxidation using peroxyacids could occur through a species resembling water oxide. Water oxide is the species formed by a 1,2-hydrogen shift in H_2O_2 ¹⁰⁶ as shown below:



The zwitterionic species in (2.17) were found to be energetically unfavorable, corroborating Bartlett's mechanism.



Bartlett's mechanism received further support from experimental results. In an elegant experiment, Woods and Beak¹⁰⁷ probed the geometric requirements for the epoxidation reaction. The peracid/olefin reagents (2.18) were synthesized as a mixture of unlabeled ($\text{C}=\text{OOOH}$) and doubly labeled ($\text{C}=\text{O}^{18}\text{O}^{18}\text{OH}$) compounds. They were then allowed to react.



By changing the length of the olefinic chain, the authors could observe whether the reaction proceeded intermolecularly or intramolecularly. When $n=1$, the reaction was observed to proceed intermolecularly and when $n=9$ the reaction proceeded mostly intramolecularly. This indicates there is a specific orientation the olefin has to assume in relation to the peracid, and that only the long chain achieves this orientation. The results support Bartlett's mechanism, where the olefin has to be oriented at 180° from the peracid.

The transition state proposed by Bartlett explains the poor enantioselective excesses observed when using chiral peroxy acids such as monoperoxycamphoric acid, since the chiral portion of the molecule stays far away from the olefin.¹⁰⁸ One example of successful enantioselective epoxidation using peracids involves the use of (+)-2-

heptaheliconitrile and 98% H_2O_2 . In this case enantiomeric excesses of up to 99.8 % were observed in the epoxidation of stilbene. It is very likely that interaction between the aromatic rings on the olefin and the peracid is responsible for the selectivity.¹⁰⁹

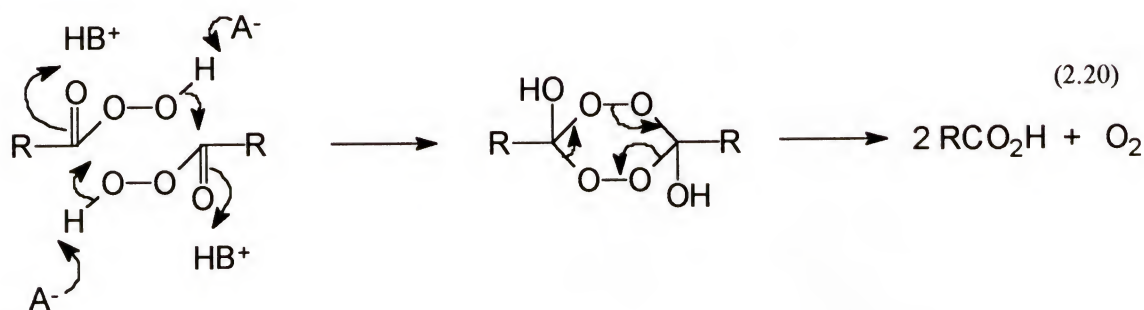
The simplified models found in the theoretical studies become more complex when solvation is considered. Solvents that form strong interactions with the peracid will disrupt the geometry of the transition state, so the peracid is no longer intramolecularly bound. Dryuk¹⁰⁴ studied the effect of adding bases such as N,N-dimethylformamide (DMF), urea or pyridine to the reaction mixture. In the presence of a base, the peracid will form an acid-base adduct (equation 2.9). It was shown that, as the basicity of the medium increased, the epoxidation rates decreased. This was valid for both the addition of bases to the reaction mixture and also when solvents of different basicities were used. Dryuk attributes this to the competition between base and olefin for complexation by the peracid (2.19).



The peracid is considered as three main parts: the carboxylic acid anion, RCOO^- , the oxygen atom being transferred and the proton. The proton is transferred to the complexed base, B. The leaving anion is protonated by HA. The transition state under these conditions must take all these species into consideration.

In the absence of olefin, the rate of decomposition of peracids is increased by the addition of bases. When an olefin is present, decomposition is inhibited. Dryuk attributed

this to the formation of a olefin-peracid complex. Decomposition can occur through the interaction of two peracid molecules with release of oxygen (2.20).

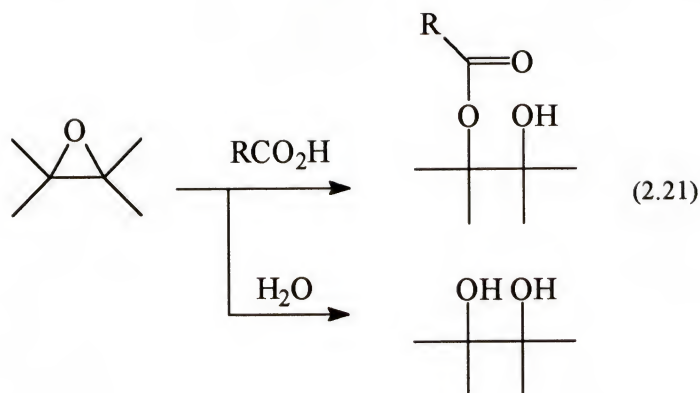


When the olefin is present, it complexes the peracid and decreases peracid-peracid interaction, inhibiting decomposition.

When a large excess of olefin is used, the rate of epoxidation becomes constant. In this case, all the peracid is complexed by the olefin, and the rate limiting step becomes the decomposition of the complex into products. The formation of this complex is dependent on the donor-acceptor properties of peracid and olefin, and on solvation interactions.

Epoxides formed by the reaction of peracids and olefins normally need to be protected from the acid catalyzed ring opening reaction. Since carboxylic acids are present after the reaction proceeds to a certain extent, care must be taken to keep the yield of epoxides high. If the epoxide cannot be removed as the reaction proceeds, buffers may be used to avoid ring opening. Ring opening can lead to diols or to carboxylates (2.20).

The acid catalyzed ring opening is the main limitation for the use of peroxycarboxylic acids for epoxidation. The generation of peracids *in situ* is subject to the slow equilibrium of the reaction between hydrogen peroxide and the carboxylic acid. If strong acids are employed to accelerate the peracid formation, they will decrease epoxide yields by ring opening.



This chapter will explore the use of in situ generated peracids in the epoxidation of olefins. The peracids are generated from carboxylic acids and anhydrides with aqueous hydrogen peroxide in the solvent N-methyl-2-pyrrolidinone (NMP). NMP is a polar solvent which is able to dissolve H_2O_2 and unfunctionalized olefins. NMP presents a high boiling point (202°C at 1 atm), which could be useful in the separation of the products. NMP has been studied by Drago and Patton¹¹⁰ and shown to be able to form a hydroperoxide with O_2 and a cobalt catalyst at 75°C , as seen in Figure 2.1. The co-product hydroxypyrrolidinone is oxidized to the succinimide, which can be hydrogenated back to NMP in the presence of ruthenium supported in carbon. NMP is known to form strong hydrogen bonds with water, which could help displace the equilibrium in equation (2.1) toward the formation of peracid.

Conditions are examined to make peracid formation catalytic with respect to carboxylic acid. This oxidant system was studied for the oxidation of both sulfides and alkenes, with and without transition metal co-catalysts. The sulfide work was published in the Ph.D. dissertation of Douglas Patton.¹¹¹ The combined work was published in the *Journal of Organic Chemistry*.¹¹²

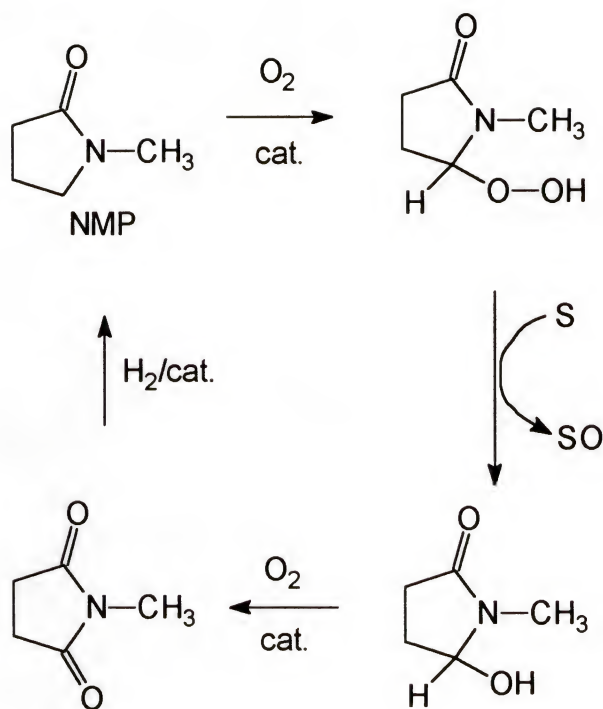


Figure 2.1. Autoxidation of N-Methylpyrrolidinone (NMP) and its use for oxidation.

Experimental

Reagents and Equipment

N-methyl-2-pyrrolidinone (HPLC Grade) was obtained from Aldrich Chemical Company and used as received. All other reagents and solvents were obtained from Fisher Scientific and used as received.

Product Analysis

All olefin reactions were carried out using o-dichlorobenzene as an internal standard. Reaction products were analyzed using an HP 5890 Gas Chromatograph. The substrate(s) and product(s) were identified and quantified using known standards.

Solutions of known concentration were prepared and used to construct calibration curves to permit quantitative determination of olefin and the corresponding epoxide.

Peroxy Acid Analysis

The peracid content in the solutions was determined as the difference of the total oxidant content and the hydrogen peroxide content. These were determined in separate titrations as follows. The total oxidant content was determined using an iodometric titration. Samples were withdrawn and diluted in 2-propanol. A saturated solution of NaI in 2-propanol and acetic acid were added and the mixture was heated to reflux for 30 seconds. The iodine was titrated with a standard sodium thiosulfate solution. The H_2O_2 content was determined using a redox titration with Ce^{4+} , using ferroin as an indicator. Samples were withdrawn and diluted in 1M H_2SO_4 that was cooled to 0 °C. They were then titrated quickly with a standardized solution of $\text{Ce}^{\text{IV}}(\text{NH}_4)_4(\text{SO}_4)_4$ in 2.5M H_2SO_4 .

Epoxidation of Olefins by Peracids

Epoxidation reactions were carried out either in a Parr pressure bottle or in a round bottom flask equipped with a cold water condenser. Care must be taken when using hydrogen peroxide solutions with 50% or greater content. Mixtures containing 30% or more of hydrogen peroxide in an organic solvent are potentially explosive. It is safest to add concentrated hydrogen peroxide to the organic solvent, not the opposite. It is advisable to keep reactions volumes to a minimum and use protective shields.

In general, anhydrides (1.0×10^{-3} moles) were allowed to react with 50 % hydrogen peroxide (3.0×10^{-3} moles) in 10 mL of NMP for 0.5 hours at room

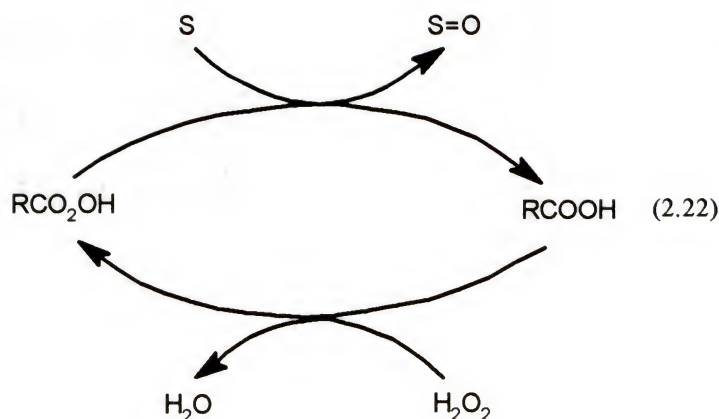
temperature. Next, 1-octene (5.0×10^{-3} moles) was added and the reaction flask placed in a silicon oil bath at 65°C . The reaction was monitored by periodic sample collection and analysis by Gas Chromatography (GC).

Results and Discussion

Previous work in our laboratory has shown that *in situ* generated peracids are able to oxidize sulfides with very good yields and rates. The conditions involved the use of maleic anhydride and 30 % aqueous hydrogen peroxide in NMP. The reaction using a ten-fold excess of maleic anhydride (MA) and a 1:1 ratio of substrate to hydrogen peroxide produces exclusively sulfoxide in 100 % yield in 15 minutes. If maleic anhydride is omitted from the reaction mixture, only a 7% conversion was observed in the same amount of time. When a 3:1 ratio of sulfide/ H_2O_2 is used, the sulfide is completely converted to the sulfone after 1 hour. An even more interesting result was obtained when the carboxylic acid is the limiting reagent. When keeping the substrate:peroxide ratio at 1:1 and increasing sulfide concentrations so a 2:1 and 3:1 ratio of substrate/carboxylic acid was used, complete conversion of the sulfide was still observed. This result implies that the carboxylic acid can be used in a catalytic fashion, as can be seen in (2.22).

The maleic acid formed after oxygen atom transfer from the peracid would react with hydrogen peroxide to regenerate the peracid. It was also found that transition metal compounds like NiCl_2 increased the rate of reaction.

In this work we will describe the use of a similar system for the epoxidation of olefins and explore the different attempts to achieve similar reactivity for the epoxidation reaction. In view of the excellent reactivity observed for sulfide oxidations, the maleic



anhydride/ H_2O_2 system described was our first choice. The liquid olefin 1-octene was selected as the substrate because of its similarity to propene, but with greater ease of handling. Terminal olefins tend to be difficult to selectively epoxidize. The epoxidation results are presented in Table 2.3. When the same conditions used for the non-catalytic sulfide oxidation are used for the 1-octene epoxidation, only a small consumption of olefin (9%) was observed after 16 hours. The epoxide peak could not be observed in this run because the maleic anhydride has similar retention times. Phthalic anhydride (PA) was used in the place of maleic anhydride under similar conditions and after three hours, no consumption of olefin or formation of epoxide was observed.

Phthalic anhydride was used for the epoxidation of 1-octene under the conditions used for the catalytic sulfide oxidations. A biphasic system resulted and no products could be observed in either of the phases after three hours of reaction. When reacting 5 mmoles of the olefin, 3 mmoles of 50% aqueous hydrogen peroxide and 1 mmole of phthalic anhydride at 65°C only one phase was observed. After three hours very little olefin disappeared and no epoxide could be found by GC. Addition of NiCl_2 did not increase the

Table 2.3. Olefin Epoxidation using *in situ* generated peracids in NMP

Run #	Olefin	Oxidant	Catalyst	Conversion	Yield	Selectivity
1 ^a	1-octene (1.6 mmol)	H ₂ O ₂ 30% (1.6 mmol)	MA (16 mmol)	9 %	---	---
2 ^b	1-octene (1.6 mmol)	H ₂ O ₂ 30% (1.6 mmol)	PA (16 mmol)	---	---	---
3	1-octene (32 mmol)	H ₂ O ₂ 50% (32 mmol)	PA (16 mmol)	---	---	---
4	1-octene (5 mmol)	H ₂ O ₂ 50% (3 mmol)	PA (1 mmol)	---	---	---
5	1-octene (5 mmol)	MMPP 2 mmol H ₂ O ₂ 50% (3 mmol)	---	26 %	23 %	88 %
6	cyclooctene (3 mmol)	H ₂ O ₂ 50% (5 mmol)	PA (2 mmol)	20 %	17 %	85 %
7	cyclooctene (3 mmol)	UHP (5 mmol)	PA (2 mmol)	37 %	34 %	92 %
8	cyclooctene (3 mmol)	UHP (5 mmol)	Phthalic Acid (2 mmol)	5 %	---	---
9 ^c	1-octene (4 mmol)	UHP 40 mmol	PA (10 mmol)	18 %	18 %	100 %
10 ^d	1-octene (4 mmol)	UHP 40 mmol	PA (10 mmol)	38 %	13 %	34 %

a - Reactions performed at 65°C in 10 ml of NMP unless indicated.

b - Reaction run in 10 ml of NMP at 25°C.

c - Reaction run in 10 ml of NMP at 40°C.

d - Reaction run in 10 ml of NMP at 80°C.

rate of epoxidation to the extent required to react at the peracid concentrations in this system.

Commercial magnesium monoperoxyphthalate (MMPP, 2 mmol), was employed as the oxidant for 1-octene (5 mmol) with 3 mmol of 50% H_2O_2 in 10 ml of NMP. In this reaction, 26% of the initial olefin was consumed and a 23% yield of epoxide was obtained after one hour. The olefin consumption corresponds to utilization of 65% of the MMPP used. None of the hydrogen peroxide reacts with the phthalate anion to regenerate the peracid at these conditions.

The poor reactivity of 1-octene in contrast to sulfide and sulfone is attributed to the poor nucleophilicity of 1-octene. Accordingly, the epoxidation of cis-cyclooctene was tried next at 65°C. Cyclooctene (3 mmol) was reacted with phthalic anhydride (2 mmol) and 50% aqueous hydrogen peroxide (5 mmol) in 10 ml of NMP. After one hour, 20% of the initial olefin was converted to the epoxide with a selectivity of 85%.

In order to increase reactivity, aqueous 50% hydrogen peroxide was substituted by the urea hydrogen peroxide adduct (UHP) in the same reaction to increase the equilibrium concentration of peracid by decreasing excess water in the system (equation (2.1)). In this reaction, 2 mmol of phthalic anhydride were added to a solution containing 5 mmol of UHP and 3 mmol of cis-cyclooctene in 10 ml of NMP. After one hour at 65°C, 37% of the initial olefin was converted to the epoxide with a selectivity of 93%.

Phthalic acid (2 mmol) was used instead of the anhydride in the oxidation of cyclooctene (3 mmol) using UHP (5 mmol) as the oxidant and 10 ml of NMP as solvent. After one hour at 65°C, little consumption of the olefin (<5%) and no epoxide

were observed. This result indicates that the epoxidation reaction would not be catalytic in anhydride.

A series of experiments were carried out in NMP using benzoic acid, 3-chlorobenzoic acid and 3,5-dichlorobenzoic acid. The purpose of these experiments was to study the regeneration step with increasingly electron withdrawing substituents. In all instances, the decrease in octene in 3 hours at 65°C was 5% or less.

The reaction of MCPBA with 1-octene was performed for comparison reasons. 5 mmoles of 1-octene were reacted with an equimolar amount of MCPBA in 15 ml of CH_2Cl_2 . After one hour of reaction, 91 % of the olefin had been consumed, being converted to the epoxide with 84 % selectivity.

Since UHP provides a good and safe source of anhydrous hydrogen peroxide and increases the conversion of cyclooctene, attempts were made to oxidize 1-octene with this system. First, 40 mmoles of UHP were reacted with 10 mmoles of phthalic anhydride in 25 ml of NMP at 40°C or 80°C. After 30 minutes, 4 mmoles of 1-octene was added and the reaction mixture kept at constant temperature. The reaction at 40°C gave an 18% decrease on the olefin and a similar increase in epoxide after three hours. The reaction at 80°C presented a 38% decrease on the olefin, but only 13 % epoxide after three hours. This difference is due to the reaction of phthalic acid and epoxide to form the carboxylate of the diol.

The more facile reaction of sulfides than alkenes with the peracid generated in this system is readily understood in terms of their nucleophilicity. Much higher concentrations of peracid are needed for epoxidation than for sulfide oxidation. These concentrations are not produced at room temperature with phthalic anhydride and 50% aqueous H_2O_2 so

little or no reaction occurs. Attempts to facilitate peracid formation by acid catalysis also catalyze ring opening hydrolysis.

Conclusions

Even though the carboxylic acid anhydride - hydrogen peroxide system showed good activity in sulfide oxidation reactions, the present work demonstrated the inability of the system to epoxidize unfunctionalized olefins in similar conditions.

The amount of peracid existing in solutions of H_2O_2 and carboxylic acid is low in the absence of strong acids. For the strong sulfide nucleophile this amount is enough for reaction and as the peracid is consumed this small amount is replenished as shown in (2.22). In the epoxidation reactions, this small concentration leads to a very slow reaction. Since the epoxide production is slow, secondary reactions of the epoxide can occur. If an acid is added to catalyze the peracid formation it also catalyzes the ring opening of the epoxide product. When a buffer is added to protect the epoxide from solvolysis, the concentration of the peracid in solution is decreased.

An increase in temperature to increase the rate of formation and the concentration of peracid in solution generated from the carboxylic acid also leads to an increase in rate of the competing epoxide reactions. Conditions can be found that lead to good yields and selectivities for the stoichiometric reaction in which peracids are generated from anhydrides reacting with H_2O_2 .

CHAPTER 3

OXIDATION OF ORGANIC COMPOUNDS IN ALKALINE MEDIA

Introduction

The use of peracids in epoxidation is widespread in organic synthesis. Meta-chloroperbenzoic acid (MCPBA) is one of the most commonly used peracids, especially for laboratory scale reactions.¹¹³ Some of the advantages of MCPBA are its commercial availability, reactivity and solubility in organic media. There are cases, however, in which a peroxy acid derived from a carboxylic acid such as MCPBA is not the most appropriate choice. After the oxygen transfer takes place, the carboxylic acid left in solution will decrease the yields of acid-sensitive epoxides by ring opening. The storage and handling of MCPBA is also difficult, since it is a shock sensitive compound. Many compounds have been proposed as substitutes for MCPBA in the literature (see Chapter 2).

In the formation of peracids from carboxylic acids and hydrogen peroxide, an acid catalyst is normally used. As we have seen in the previous chapter, this has a deleterious effects on the yields of epoxides when the peracid generation is performed at the same time as the epoxidation reaction.

The formation of peroxy acids can also be performed in basic solution. A method using alkaline hydrogen peroxide for the synthesis of monoperoxyphthalic acid has been described.¹¹⁴ After the reaction is complete, the solution is acidified and the peracid is

extracted to an organic solvent. An improved method was described by Payne and used sodium carbonate as the base instead of sodium hydroxide.¹¹⁵ The use of carbonate decreases decomposition of the peroxide and a smaller excess of peroxide can be used.

Magnesium monoperoxyphthalate is prepared by the reaction of phthalic anhydride and MgO (also possible with Mg(OH)₂ or MgCO₃) and hydrogen peroxide.¹¹⁶ Other anhydrides can be used, such as maleic anhydride and cyclohexane dicarboxylic acid anhydride. When a diprotic acid is converted into the peracid, the C(O)OOH group is the least acidic of the two groups. In this instance there is a chance for the carboxyl group to be deprotonated while the peracid group remains in the acid form. This is true for the salt magnesium monoperoxyphthalate(MMPP). Each monoperoxyphthalate has one negative charge being balanced by the Mg²⁺ ion and they retain the CO₃H group proton. This is important for the epoxidation reaction, since we have the possibility of forming the internal hydrogen bond suggested for the transition state during oxygen atom transfer.

The Chemistry of Peroxocarbonates

Carbonic acid, H₂CO₃, is a diprotic acid like phthalic acid. The hydrogen monoperoxocarbonate anion can be generated through the reaction of hydrogen peroxide and sodium hydrogen carbonate (3.1):



Studies are underway to determine the equilibrium constants for the reaction and how solvent effects contribute to the peracid formation. The mono hydrogen

peroxocarbonate anion has been shown to be able to perform the oxidation of sulfides to sulfoxides and sulfones.¹¹⁷ In this chapter we will describe our attempts to perform the epoxidation reaction using the peracid derived from hydrogen peroxide and the hydrogen carbonate anion.

There have been very few reports of the synthesis of peroxocarbonates in the literature, even though researchers have been interested in the reaction between hydrogen peroxide and carbonates since the end of the 19th century. In 1950, Partington and Fathallah¹¹⁸ reinvestigated the contradictory results obtained up to that time. Several compounds with different alkali-metals were isolated from the reaction and analyzed by elemental analysis techniques, the only techniques available at the time.

In 1980, Griffith and Jones prepared several alkali-metal peroxocarbonates in the solid state.¹¹⁹ Based on spectroscopic evidence, they distinguished two classes of compounds. The perhydrates contain hydrogen peroxide crystallized as an adduct from the parent carbonates and H₂O₂. The perhydrate formed by crystallization of solutions of sodium carbonate and hydrogen peroxide is commercially known as "sodium percarbonate" or SPC. The chemistry of SPC in water is basically that of alkaline hydrogen peroxide, with any enhancements on the rate by the use of carbonate being attributed to the formation of HCO₄⁻.⁸⁹ SPC is used in organic solvents as a source of anhydrous hydrogen peroxide, mainly for the generation of peracids which then perform the oxidation.⁸⁸

The second class includes the true peroxocarbonates which present a C-O-O linkage and can result either from the electrochemical oxidation of carbonates or the reaction of an alkali-metal hydroxide, CO₂ and hydrogen peroxide. This class can be

further separated in the peroxocarbonates and the peroxodicarbonates. These structures are shown in Figure 3.1.

Potassium peroxodicarbonate can be prepared by the reaction of KOH, CO₂ and H₂O₂ at -20 °C or by the anodic oxidation of saturated K₂CO₃ at -20 °C. These salts are very hygroscopic and decompose thermally releasing CO₂ and O₂.¹²⁰ The authors were unable to perform oxidations using these salts since they decompose very fast in water and they were unable to dissolve them in crown ethers. In 1986 Griffith, Skapski and co-workers studied the peroxocarbonate equilibrium in aqueous solution.¹²¹ Spectroscopic evidence (solution Raman and ¹³C NMR) suggests the existence of a pH dependent equilibrium between HCO₄⁻ and CO₄²⁻, in solutions of HCO₃⁻ and excess H₂O₂. The results can be summarized as follows: below pH 7, CO₂ is evolved from the bicarbonate; above pH 7 the ¹³C resonance attributed to the peroxocarbonate increases until it reaches equilibrium, the rate of which depends on the pH and the temperature. Dissolution of the NaH¹³CO₄·H₂O or K₂¹³C₂O₆ in water results in fast decomposition. When the same solids are dissolved in 4 M H₂O₂, the same resonance as seen on the HCO₃⁻/H₂O₂ mixture is immediately observed. The following equilibria are proposed for the system:



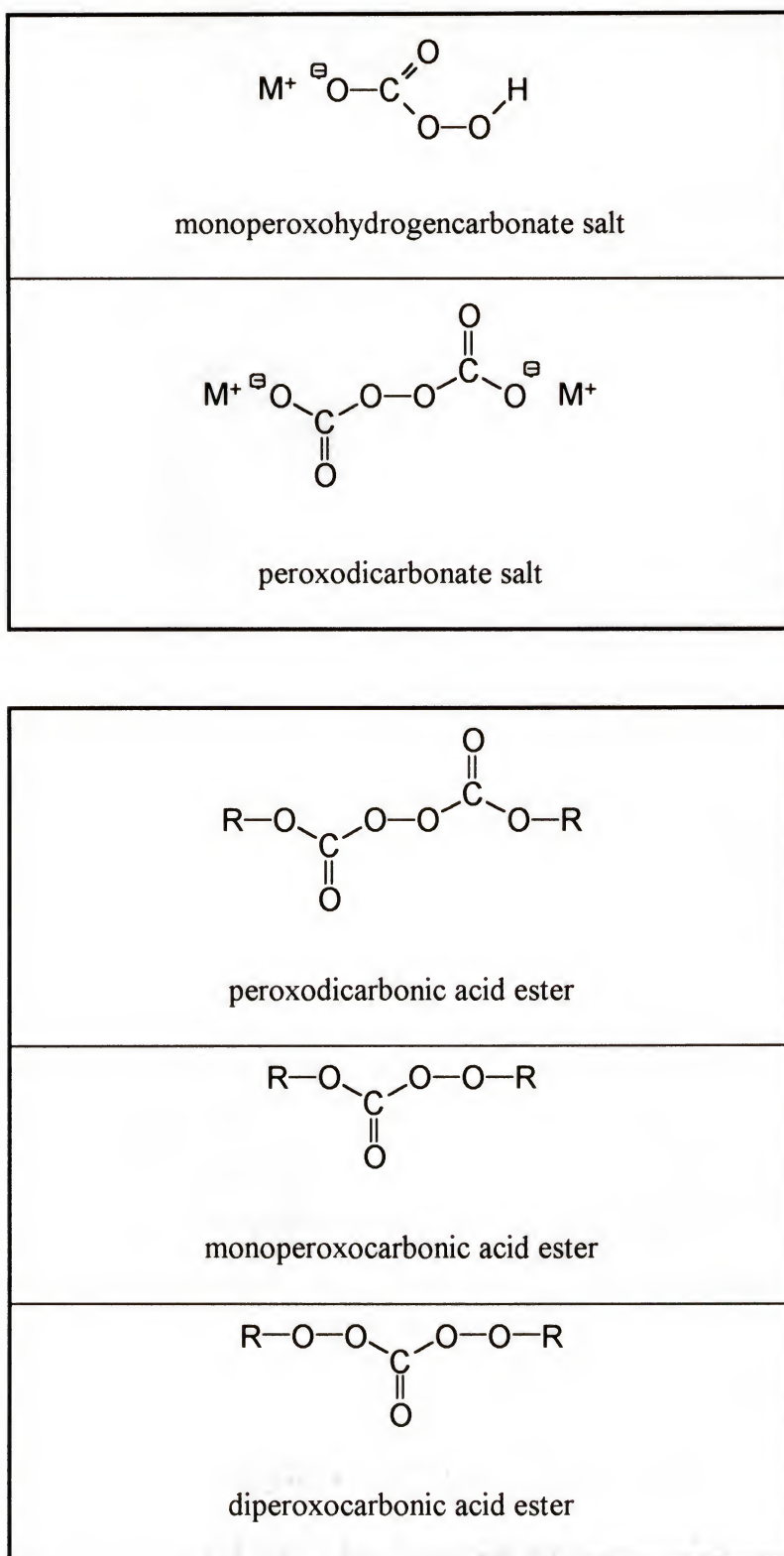
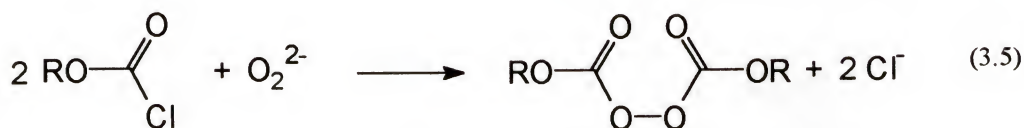


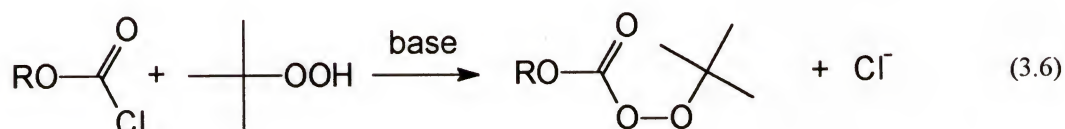
Figure 3.1. Structures of peroxocarbonate species

The major percarbonate species found in solution is proposed to be HCO_4^- .

Esters of the peroxodicarbonic acid have been synthesized by the reaction of chloroformates and aqueous sodium peroxide:¹²²



The esters of the monoperoxocarbonic acid were synthesized by the reaction of t-butyl hydroperoxide and either chloroformates or phosgene (equations (3.6) and (3.7)).



These compounds were not used for oxidations but were shown to be active catalysts for the polymerization of certain monomers. Coates and Williams synthesized o-benzylmonoperoxycarbonic acid by the perhydrolysis of dibenzyl peroxydicarbonate.¹²³ This compound is active for the epoxidation of olefins, releasing CO_2 and benzyl alcohol. The reaction medium remains essentially neutral, avoiding the side reactions seen in the case of carboxylic acids.

The use of peroxocarbonates for the oxidation of organic compounds deserves investigation. Such a system would have several advantages in relation to the use of

peroxycarboxylic acids. The very low price of NaHCO_3 makes its use for large scale activation of hydrogen peroxide very attractive. The neutral/alkaline solutions can protect acid-sensitive products such as epoxides. The oxidations can be performed without the need for chlorinated solvents. The use of these solvents is an environmental problem due to very toxic organochlorinated by-products that can be formed.

Generation of Peroxyacids from Precursors

We also describe the use of hydrogen peroxocarbonates in the generation of peracids by their reaction with a series of peracid precursors. The first system studied involves the perhydrolysis of esters. A system based on the alkaline perhydrolysis of an ester would present several advantages when compared to the acid-catalyzed peracid generation from the carboxylic acid and hydrogen peroxide. The reaction steps involved are shown in Figure 3.2. After the reaction is completed, the alcohol and the carboxylic acid can be recycled back to the ester by acidifying the medium and removing the water.

Very few studies have been performed on the perhydrolysis of esters. Lipases have been used as catalysts for the synthesis of peracids from carboxylic acids and hydrogen peroxide.⁹³ The enzyme was immobilized on an acrylic resin and is available commercially as Novozym 435[®]. It was later found that the same enzyme catalyzes the perhydrolysis of esters by H_2O_2 and *in situ* epoxidations were carried out with a large number of straight chain carboxylic acids and esters.¹²⁴ This system has also been used for Baeyer-Villiger oxidations¹²⁵ and the "self"-epoxidation using unsaturated fatty acids.¹²⁶ The enzyme was found to be active for the transesterification, and as in the perhydrolysis case trifluoromethyl esters were found to be better substrates. The system has also

recently been used for the synthesis of epoxyalkanoacylates, where allylic alcohols and esters undergo transesterification and perhydrolysis simultaneously.¹²⁷

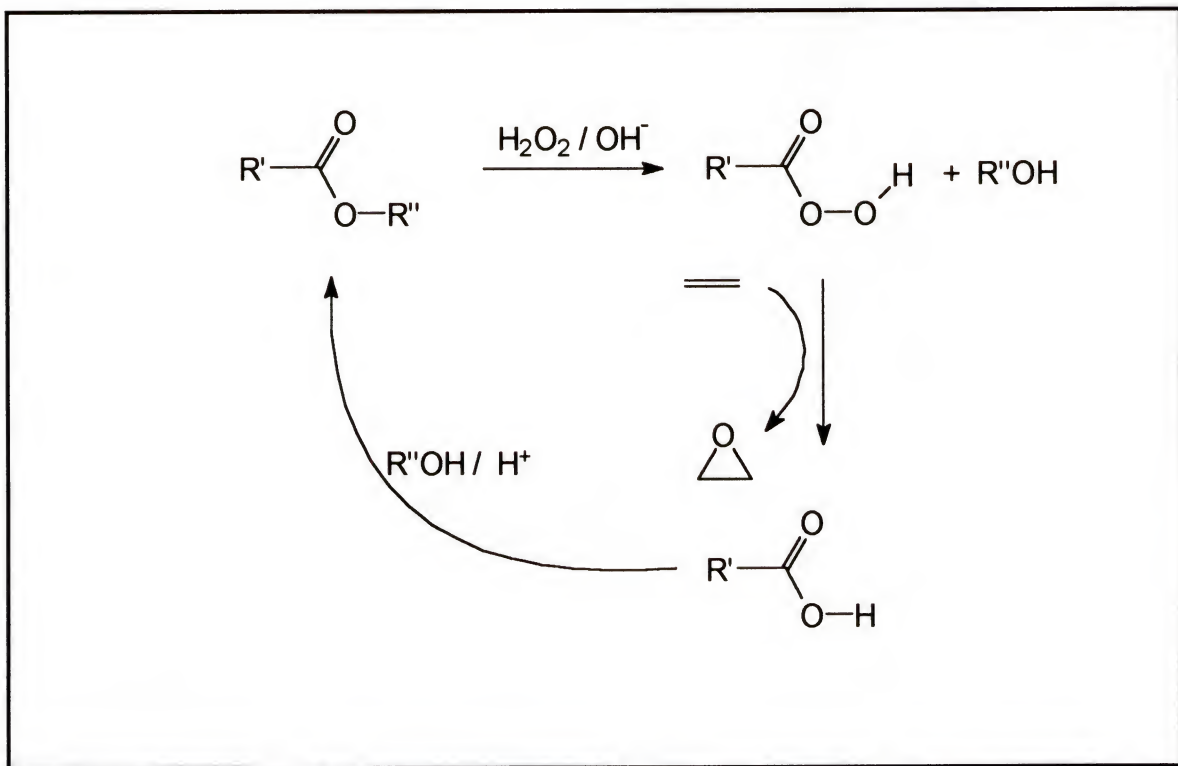


Figure 3.2 - Perhydrolysis of esters in alkaline media.

A large number of esters have been described in the patent literature as peracid precursors for use in the bleaching industry. Some examples are illustrated in Table 3.2. If a peracid is used in the composition of granular bleaching products, decomposition will take place leading to loss of the active oxygen content. If, on the other hand, a peracid precursor is used together with a stable source of peroxide, a more enduring composition is obtained. The peroxide is normally introduced in the composition as sodium perborate or sodium percarbonate. Even though hydrolysis of the ester can be performed by the hydroxyl ion, the perhydroxyl ion is a much better nucleophile and good yields of the peracid can be obtained even in the low concentrations of peroxide used in washing.

Table 3.1. General structures for peroxy acid precursors used in the bleaching industry.

Precursor*	Peracid	Reference
		128
		129
		130
		131
		132

* L = leaving group

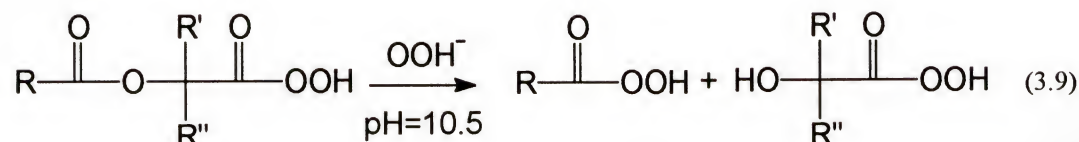
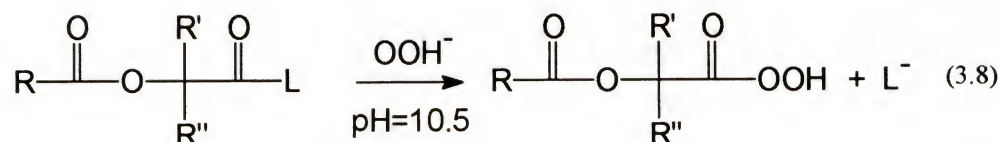
Q⁺ = nitrogen or phosphorus

Z⁻ = inert anion to balance Q⁺

X = either a heteroatom or nothing

When a glycolate ester is used, two different peracids may be obtained under the right conditions by consecutive perhydrolysis of the precursor (equations 3.8 and 3.9).

One example of a leaving group in this system is sodium phenylsulphonate.¹³²



These systems are used for the removal of stains in fabrics and are used in conjunction with detergents and emulsifiers which keep the pH in the alkaline range.

The second system studied involves the generation of peracids from the respective anhydrides and the hydrogen carbonate/hydrogen peroxide system. Similar systems have been reported for epoxidations under anhydrous conditions using hydrogen peroxide adducts such as UHP and SPC. The adducts release the hydrogen peroxide slowly so the peroxyacid is used as it is produced. SPC was used in conjunction with trifluoroacetic acid for the Baeyer-Villiger oxidation of ketones to esters.¹³³

The last system studied describes the generation of peroxyacids from nitriles and the hydrogen carbonate / hydrogen peroxide system. This system was described in Chapter 2 and has also been used in conjunction with hydrogen peroxide adducts for the oxidation of organic substrates.

Peroxy acids can also be generated by the autoxidation of aldehydes, as seen in Chapter 2. We decided to investigate the possibility of generating organic percarbonic acids through this route. In this case, the autoxidation of methyl formate would lead to

the formation of methyl percarbonic acid, as shown in Figure 3.3. The use of methyl formate as a solvent for the epoxidation of olefins has been disclosed in a patent.¹³⁴ The process described does not require catalysts or initiators but uses high pressure of dioxygen and high temperature. The conversion for propylene oxidation in a variety of solvents was very similar (around 20-25 %) but the selectivity for epoxide changed from around 50 % for methyl formate to around 30 % for other esters (ethyl and butyl formate, methyl and ethyl acetate, dimethyl carbonate). No explanation was given for the difference in selectivities observed. The use of initiators such as organic peroxides reduced the induction time but had no influence in the selectivity to epoxide.

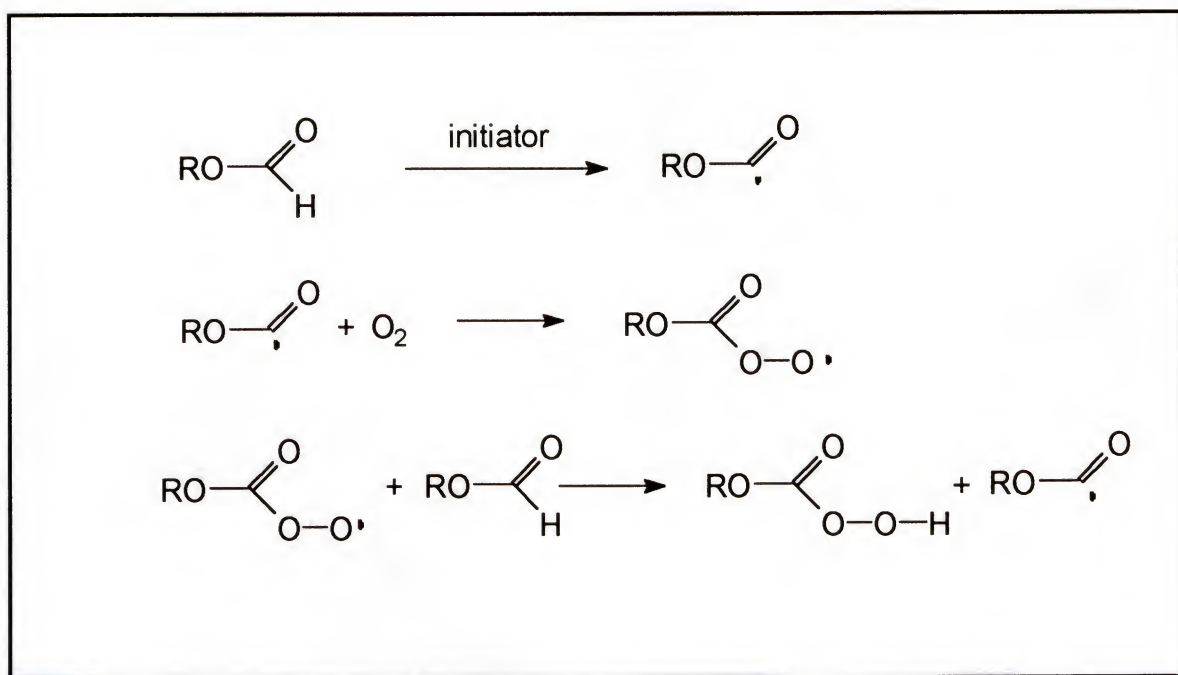


Figure 3.3. Percarbonic acid formation with alkyl formates.

Experimental

Reagents

All of the esters and olefins were obtained from Aldrich Chemical Company and used as received. High purity sodium hydrogen carbonate (99.99+ %, Aldrich) was used to avoid any metal contamination. Hydrogen peroxide 70 % (technical grade) was graciously provided by Solvay Interlox Inc. and used without further purification. All other reagents and solvents were obtained from Fisher Scientific and used as received.

Product Analysis

All olefin reactions were carried out using decane or o-dichlorobenzene as an internal standard. Reaction products were analyzed by gas chromatography (GC) using an HP 5890 GC equipped with a 30 m HP 50+ (Crosslinked 50 %Ph-Me-silicone) column using helium as the carrier gas. The substrate(s) and product(s) were identified and quantified using known standards. Error values for epoxide yields were estimated from triplicate runs on the epoxidation of cyclooctene by hydrogen peroxide using methyl formate as the solvent/peracid precursor and sodium hydrogen carbonate as base promoter. The error limits are assumed to be similar for the other reactions reported in this chapter. All epoxide yields reported are derived from GC data only, except when noted.

Epoxidation of Olefins by Peroxocarbonate Salts Generated *in situ*

The procedure for the reactions involved dissolving the olefin in the solvent together with the internal standard in a capped vial equipped with a septum and a needle to vent gases. The hydrogen carbonate salt was dissolved in the 50 % aqueous hydrogen peroxide solution separately and this solution was added to the olefin mixture. Samples were withdrawn at different times and analysed by GC as noted.

Typical reaction conditions are shown below:

Olefin : 10 mmol

NaHCO₃ : 1 mmol (0.084 g)

H₂O₂ 50% : 34 mmol (2.0 mL) - pH adjusted to ~7 using NH₄OH.

Solvent : 5 mL

Internal standard : 0.1 mL

Synthesis of Sodium Hydrogen Monoperoxocarbonate Monohydrate, NaHCO₄.H₂O

The synthesis was performed according to procedure reported in the literature.¹¹⁹

A solution of aqueous hydrogen peroxide 50 % (5 mL) was placed in a salt-ice bath at -20°C. A cooled solution of sodium hydroxide (2.8 g, 70 mmol) in water (10 mL) was added slowly dropwise with stirring. A small amount of white precipitate appeared. The salt-ice bath was replaced by an ice bath at 0°C and the precipitate dissolves. At this point a CO₂ stream is passed over the surface of the mixture for 35 minutes. After this period a thick white precipitate formed. The precipitate was filtered under reduced pressure, washed with small portions of cold absolute ethanol and ether and further dried under vacuum. An iodometric titration of the dried solid found 25.8 % w/w active oxygen (calculated for NaHCO₄.H₂O 27.2%).

Synthesis of Tetrabutylammonium Hydrogen Carbonate

Tetrabutylammonium hydrogencarbonate was adapted from the synthesis of tetramethylammonium hydrogencarbonate described in the literature.¹³⁵ A solution of tetrabutylammonium hydroxide in methanol (Aldrich, 1.0 M) was diluted in methanol and saturated with CO₂ for 40 minutes. After this period the solution was rotary evaporated to remove the solvent, yielding a white, very hygroscopic solid. The solid was kept in a closed flask under nitrogen until use.

Epoxidation of Olefins by Peroxy Acids Generated by the Perhydrolysis of Precursors

Reactions were performed at room temperature in capped vials equipped with a septum and a needle for venting gases. Samples were withdrawn at different times and analysed by GC as noted. Typical reaction conditions are shown below:

Olefin : 5 mmol

NaHCO₃ : 1 mmol (0.084 g)

H₂O₂ 50% : 34 mmol (2.0 mL) - pH adjusted to ~7 by addition of NH₄OH

Solvent (alkyl ester or methanol): 5 mL

Internal standard : 0.1 mL

Great care must be taken when handling alkyl formate solutions. Both methyl and ethyl formate are very flammable and skin irritants. Avoid all contact with liquid and vapors.

Results and Discussion

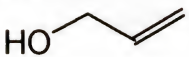
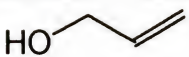
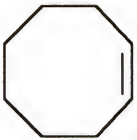
Epoxidation of Olefins using Hydrogen Carbonate

As discussed in the introduction, alkaline-metal hydrogen carbonates can form peroxy species by reaction with hydrogen peroxide. These species were studied in our laboratory and were found to be very reactive for the oxidation of alkyl sulfides. As an example, in the oxidation of ethyl phenyl sulfide using monoperoxo hydrogencarbonate generated *in situ*, the half-life of the reaction was found to be 4.5 minutes.¹¹⁷ The success with the sulfide oxidations led us to attempt the epoxidation of olefins with a similar system.

We searched for a suitable solvent that would be resistant to oxidation and that at the same time would bring the hydrogen carbonate into solution in the presence of the very non-polar olefin and aqueous hydrogen peroxide, while keeping all components in one phase. Preliminary attempts using the same solvents as used in the sulfide system proved unsuccessful, as shown in Table 3.2. When methanol and t-butanol are used, the solubility of the sodium hydrogen carbonate is very low, and no epoxidation of norbornene is observed. A water soluble olefin, allyl alcohol, was used in an attempt to increase the polarity of the medium. When methanol and t-butanol were used for the epoxidation of allyl alcohol, a clear solution resulted, with all of the sodium hydrogen carbonate dissolved. Still, no epoxidation of allyl alcohol was observed, even after 24 hours of reaction.

The effect of the cation on the reactivity was studied. To increase the anion solubility, a quaternary ammonium alkyl group was used as the counter ion for the

Table 3.2. Epoxidation of olefins using hydrogen monoperoxocarbonate generated *in situ*.

Solvent (5 mL)	Olefin (5 mmol)	HCO ₃ ⁻	H ₂ O ₂ (50 %)	Reaction time (hours)	Yield epoxide
Methanol		Na ⁺ , 1 mmol	34 mmol	2	-----
t-Butanol		Na ⁺ , 1 mmol	34 mmol	2	-----
Methanol		Na ⁺ , 1 mmol	34 mmol	2	-----
t-Butanol		Na ⁺ , 1 mmol	34 mmol	2	-----
Methanol		Na ⁺ , 5 mmol	34 mmol	2	-----
Methanol		Bu ₄ N ⁺ , 2 mmol	34 mmol	2	< 1 %
Methanol		Na ⁺ , 5 mmol + Aliquat 336, 2 mmol	34 mmol	2	-----

hydrogen carbonate. Tetrabutylammonium hydrogen carbonate was synthesized using a modified procedure reported in the literature. The epoxidation of cyclooctene (5 mmol) was attempted using methanol as the solvent (5 mL), 50 % hydrogen peroxide (2 mL, 34 mmol), and 2 mmol of the tetrabutylammonium hydrogen carbonate. The reaction mixture was homogeneous but a very small conversion to epoxide was observed (<1 % of the initial olefin).

Aliquat 336[®] (tricaprylmethylammonium chloride) is a commonly used cationic phase transfer catalyst. The epoxidation of norbornene (5 mmol) was examined, using dichloromethane as the solvent (5 mL), sodium hydrogen carbonate (5 mmol) and 70 % hydrogen peroxide (1 mL). The resulting mixture was biphasic. No epoxide was observed in either phase after 2 hours, with or without the addition of Aliquat (2 mmol) to the system.

The fact that the monoperoxohydrogencarbonate anion is able to oxidize sulfides but not olefins in similar conditions can be explained by the higher nucleophilicity of the sulfides. The equilibrium concentration of the HCO_4^- ion may not be high enough for the reaction to proceed in the experiments outlined so far. If this is the case, we may be able to perform the oxidation of olefins if we start with a large enough amount of the HCO_4^- ion. To verify this, the synthesis of sodium hydrogen monoperoxocarbonate was performed following the literature procedure.¹¹⁹

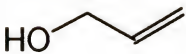
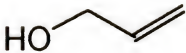
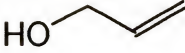
Sodium hydrogen monoperoxocarbonate (10 mmol) was added to a solution of norbornene (5 mmol) in methanol (5 mL). The mixture was stirred for 2 hours, during which no epoxide formation was observed. Most of the solid peroxocarbonate remained

undissolved. A second reaction was attempted where the same amounts of reagents were used and 0.5 mL of hydrogen peroxide 70 % was also added. Again very little dissolution and no epoxide was observed.

Similar reaction conditions were used in an attempt to epoxidize allyl alcohol. Using methanol (5 mL) as the solvent, NaHCO_4 (10 mmol) was mixed with allyl alcohol (5 mmol). No epoxide was observed in 2 hours of reaction. The same reaction was run with the addition of 1 mL of 50 % H_2O_2 to increase the stability of the monoperoxohydrogencarbonate, but the result was still negative. Finally, a third reaction was attempted where the allylic alcohol was used as the solvent (5 mL), still with no epoxide formation.

The results and conditions for these epoxidation attempts are given in Table 3.3. We can conclude from all of these experiments that the hydrogen monoperoxocarbonate anion is not able to perform epoxidation of olefins by itself. This behavior contrasts with the reactivity of organic peroxocarbonic acids and with the monoperoxyphthalate anion, both of which are able to perform epoxidations. One possible explanation is that the hydrogen carbonate is strongly solvated by the alcohol/water solvent and the non-polar olefin cannot get to the anion. This would imply that in the case of monoperoxyphthalate the olefin is more accessible to the oxidant. This explanation would not, however, account for the non-reactivity toward allyl alcohol, which is water soluble. Allyl alcohol is a deactivated olefin, since the hydroxyl group removes electron density from the double-bond. It is possible that a more reactive, water soluble olefin could be oxidized by the hydrogen carbonate/ hydrogen peroxide system. Quinones and other electron deficient

Table 3.3. Epoxidation of olefins using synthesized sodium hydrogen monoperoxocarbonate.

Solvent (5 mL)	Olefin (5 mmol)	NaHCO ₄ .H ₂ O	H ₂ O ₂ (50 %)	Reaction time (hours)	Yield, epoxide
Methanol		10 mmol	34 mmol	2	-----
Methanol		10 mmol	-----	2	-----
Methanol		10 mmol	34 mmol	2	-----
Methanol		10 mmol	-----	2	-----
 Allyl Alcohol		10 mmol	34 mmol	2	-----

unsaturated compounds are good candidates for this, since they are easily epoxidized by alkaline hydrogen peroxide (see Chapter 2).

Epoxidation of Olefins by Peroxy Acids Generated by the Perhydrolysis of Esters

Esters can serve as both reactant and solvent for the epoxidation of olefins with the hydrogen peroxide/ hydrogen carbonate system. When a reactive ester such as an alkyl formate is used as the solvent, moderate to high yields of epoxides can be obtained. As discussed in the introduction, the perhydrolysis of esters leads to the formation of peroxy acids. Cyclooctene (5 mmols) was dissolved in methyl formate (5 mL) and a solution of sodium hydrogen carbonate (1 mmol) in 50 % aqueous hydrogen peroxide (1.0 mL, 17 mmol) was added. After 90 minutes, almost all of the cyclooctene was consumed and cyclooctane oxide was produced with very good yields (4.85 mmol, 97 % selectivity). To better study the reaction, it was repeated on a larger scale, to observe the co-products of the solvent oxidation. To this effect, 20 mL of methyl formate was mixed with 20 mmol of cyclooctene (1.95 mL) and 5 mmol of sodium hydrogen carbonate dissolved in 4 mL of 50 % hydrogen peroxide was added. After 1.5 hours the cyclooctene had completely converted to epoxide. At this time the pH of the medium was markedly acidic as determined by indicator paper and the solution was completely homogeneous. 20 mmol of sodium hydrogen carbonate (1.68 g) was added to neutralize the acid and the excess peroxide was decomposed by addition of a minimal amount of MnO_2 . The mixture was filtered to remove the MnO_2 and evaporated to dryness. The dry residue was extracted with ethyl ether, leaving a white solid. Analysis of this white solid by infrared spectroscopy determined it to be sodium formate and the amount corresponded to

approximately 17 mmols. The organic extract was rotary evaporated yielding cyclooctene epoxide, 18 mmols. From this experiment we can conclude that the methyl formate is undergoing perhydrolysis, forming performic acid and methanol. The performic acid is the active epoxidizing species, yielding formic acid after oxygen atom transfer. This will decrease the pH once the buffer capacity of the hydrogen carbonate is exceeded and it is converted into CO_2 . If care is not taken to replenish the buffer, the continued hydrolysis of the solvent will generate enough acid to open the epoxide ring, decreasing yields.

The epoxidation of norbornene was used to probe some reaction conditions. In the absence of sodium bicarbonate or any another base there was no epoxide formation in 2 hours. If, on the other hand, 1 mmol of sodium hydrogen carbonate is added under the same conditions, 66 % of the initial olefin is converted to the epoxide in only 30 minutes.

Initially, the perhydroxyl ion or the hydrogen monoperoxocarbonate ion attacks the ester, producing peroxyformic acid. After the epoxidation step is completed, the formic acid liberated will react with the base, buffering the medium. If the base, hydrogen carbonate in this case, is present in less than stoichiometric amounts, the medium eventually becomes acidic. This increases the rate of perhydrolysis of the ester, forming more performic acid from the excess hydrogen peroxide. If the medium becomes too acidic, however, the yields of epoxide will be compromised.

One way to avoid this problem would be to run the reaction with excess olefin and limit both the hydrogen peroxide and the peroxy acid precursor. In this case the peracid precursor would be converted to the carboxylic acid salt once the reaction is over and the excess olefin could be recycled. Cyclooctene (5 mL) was mixed with 5 mmol (0.30 mL)

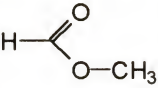
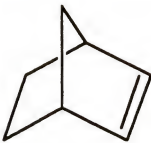
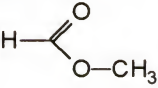
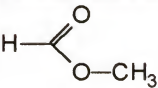
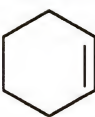
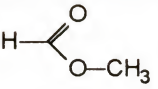
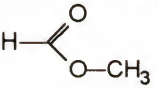
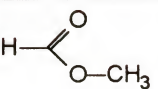
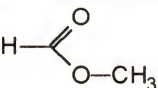
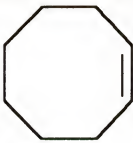
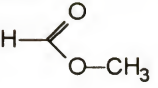
of methyl formate and 5 mmol of hydrogen peroxide 50 %. Tetrabutylammonium hydrogen carbonate (10 mmol) was chosen as the base for this reaction, since the non-polar olefin is being used as the solvent. The resulting mixture was biphasic. After 5 hours, only approximately 0.5 mmols of cyclooctene epoxide were produced. The slow rate of reaction shows that it is the large excess of the ester that drives the reaction to completion.

To probe the factors that influence this reaction, several olefins were epoxidized using this method. The results are displayed in Table 3.4.

To further study the effect of the solvent on the reaction, a water miscible olefin, allyl alcohol was chosen as substrate. Allyl alcohol (10 mmol) was dissolved in 5.0 mL of methyl formate. A solution of sodium hydrogen carbonate (1 mmol) in 2 mL of 50 % aqueous hydrogen peroxide (34 mmol) was added and the system closed. The solution was homogeneous with no solid sodium bicarbonate present. The yield of glycidol increased from 4.5 % in 1 hour to 48 % in 30 hours. There were no side products detectable by GC.

In a similar procedure, 1-octene was used as the substrate for epoxidation. In this reaction methyl trifluoroacetate (DANGER! Very corrosive and toxic!) was used as the peracid precursor. Terminal olefins such as 1-octene are much more difficult to epoxidize, requiring a stronger oxidizer. The trifluoroperacetic acid is a very potent oxidizing agent and has been used for the epoxidation of 1-octene with success, in the presence of buffers. In a reaction using methyl trifluoroacetate (1 mL, 10 mmol) in methanol (5 mL), all of the 1-octene (5 mmol) was consumed in a very short time, but no epoxide was found in the solution, due to the resulting acidity. A different procedure was devised to try to isolate

Table 3.4. Epoxidation of olefins using methyl formate as peracid precursor.

Solvent (5 mL)	H ₂ O ₂ (50 %)	Base	Olefin	Time (hours)	Yield (± 5 %)
	34 mmol	NaHCO ₃ , 1 mmol	 5 mmol	0.5	66 %
	34 mmol	-----	 5 mmol	2	-----
	34 mmol	NaHCO ₃ , 1 mmol	 5 mmol	2	42 %
	34 mmol	NaHCO ₃ , 1 mmol	 5 mmol	24	32 %
	34 mmol	NaHCO ₃ , 1 mmol	 5 mmol	24	49 %
	34 mmol	NaHCO ₃ , 1 mmol	 5 mmol	1.5	97 %
	34 mmol	Na ₂ HPO ₄ , 5 mmol	 5 mmol	1.5	20.5 %
	34 mmol	Bu ₄ NHCO ₃ , 2 mmol	 5 mmol	3	24 %

the epoxide being formed from the strong carboxylic acid. The olefin, 1-octene (5 mmol) was dissolved in CHCl_3 (5 mL) together with the internal standard (o-dichlorobenzene) and methyl trifluoroacetate (3 mL, 30 mmol). In a separate vial sodium hydrogen carbonate (0.84 g, 100 mmol) was dissolved in 70 % aqueous hydrogen peroxide. The solutions were combined, yielding a biphasic system. The methyl trifluoroacetate can react with the hydrogen peroxide/hydrogen carbonate system in the aqueous phase and form the trifluoroperacetic acid. The peracid is soluble in the organic phase and will then react with the olefin, forming epoxide and trifluoroacetic acid. The trifluoroacetic acid is water soluble and once in the aqueous phase will react with the sodium hydrogen carbonate, releasing CO_2 and forming the salt. As long as there is hydrogen carbonate in the aqueous phase, the pH will not drop and the epoxide is safe. After 2 hours at room temperature, 25 % of the initial 1-octene had been converted to the epoxide. The system is depicted in a schematic way in Figure 3.2.

Other esters were used as peroxy acid precursors for the epoxidation of olefins. Methyl acetate was used for the epoxidation of cyclohexene, yielding only 10 % epoxide after 1.5 hour. The resulting peracetic acid is not as strong a oxidizing agent as the performic acid or the trifluoroperacetic acid. An ester of phthalic acid, methyl phthalate was used in the epoxidation of cyclooctene. No epoxide formation was observed in this system. The result is not surprising in view of the fact that no aromatic esters undergo perhydrolysis in the enzymatic systems described in the literature.

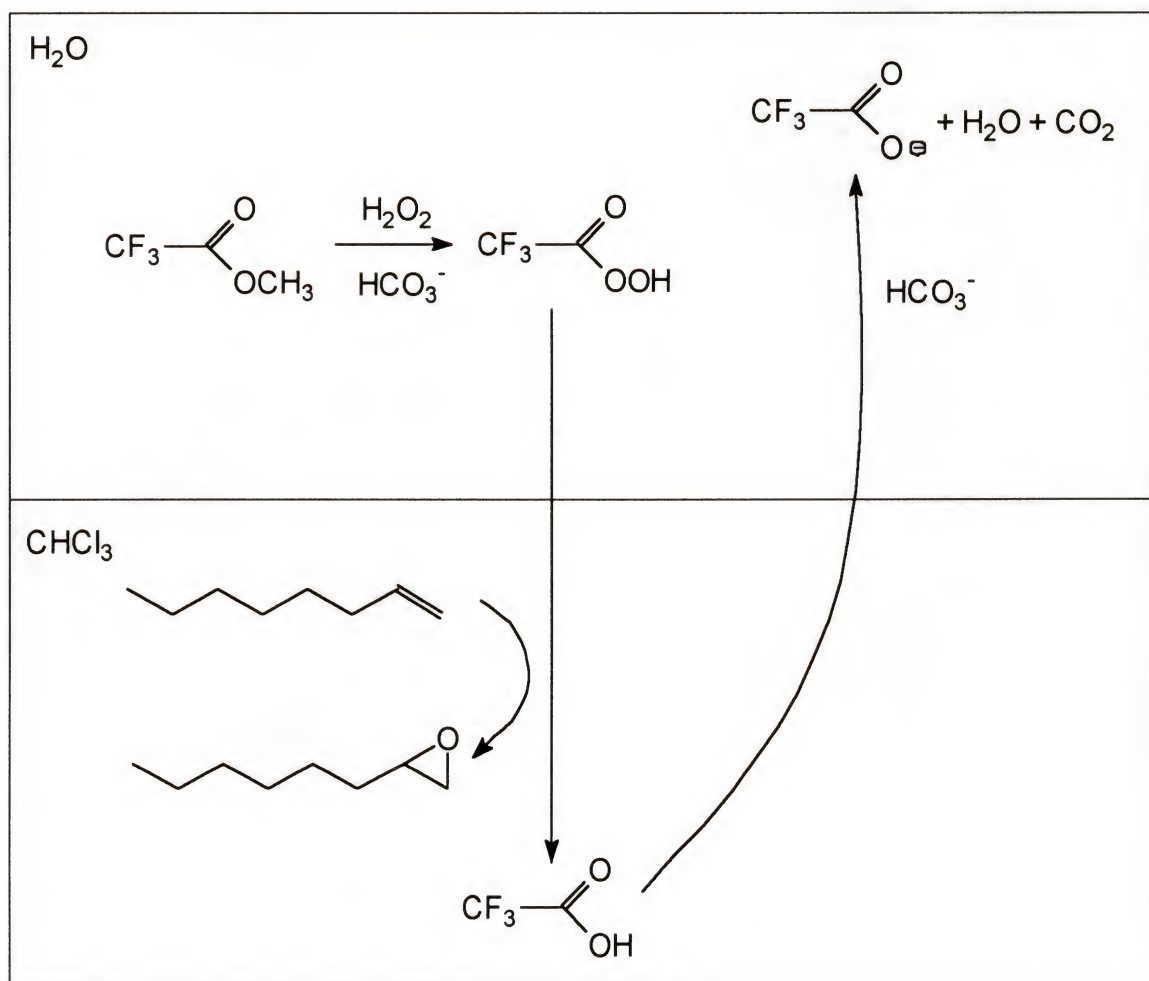
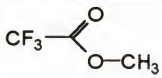
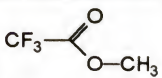
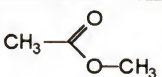
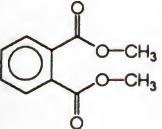
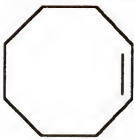


Figure 3.2. Biphasic epoxidation of 1-octene by methyl trifluoroacetate.

Table 3.5. Epoxidation of olefins using other alkyl esters.

Ester	H ₂ O ₂	HCO ₃ ⁻	Olefin	Time (hours)	Yield (± 5 %)
 10 mmol in CH ₃ OH	34 mmol	5 mmol, Na ⁺	 5 mmol	0.5	-----
 30 mmol in CHCl ₃	42 mmol	10 mmol, Na ⁺	 5 mmol	2	25 %
	34 mmol	1 mmol, Na ⁺	 5 mmol	1.5	10 %
	34 mmol	1 mmol, Na ⁺	 5 mmol	2	-----

Epoxidation of Olefins by Peroxy Acids using Acid Anhydrides and $\text{H}_2\text{O}_2 / \text{HCO}_3^-$

Acid anhydrides were used as additives for the epoxidation of olefins with the hydrogen peroxide/ hydrogen carbonate system. Phthalic anhydride was chosen for these reactions due to our prior work in neutral/acidic solution (Chapter 2). The monoperoxyphthalic acid is known to be able to perform epoxidations as the magnesium salt, as long as it is soluble in the medium. The first reaction tried was the epoxidation of cyclooctene in stoichiometric conditions. Phthalic anhydride (5 mmol, 0.74 g) was dissolved in a methanol solution (10 mL) containing cyclooctene (5 mmol, 0.65 mL) and the internal standard (o-dichlorobenzene, 0.1 mL). The reaction was initiated by the addition of 10 mmol of aqueous H_2O_2 70% where 5 mmol NaHCO_3 (0.42 g) was dissolved. There was a rapid evolution of gas and after 90 minutes 72 % of the initial olefin was converted to the epoxide (as determined by GC). This reaction has as driving force the opening of the phthalic anhydride ring and the release of CO_2 from the hydrogen carbonate. This reaction can be compared to a similar run where the hydrogen carbonate was omitted. Results of both runs are displayed in Table 3.6. It can be seen that the presence of the sodium hydrogen carbonate increased the yield of epoxide almost three fold within the same reaction time.

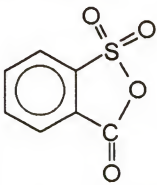
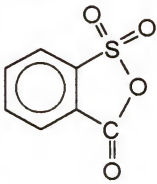
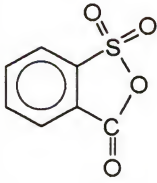
A biphasic system was also used, trying to take advantage of the faster rates observed in chlorinated solvents. Phthalic anhydride (5 mmol) was dissolved in dichloromethane (5 mL) together with cyclooctene (5 mmol). Hydrogen peroxide (10 mmol) and tetrabutylammonium hydrogen carbonate (5 mmol) were added. After 30 minutes the observed yield of epoxide was 67 % of the initial olefin.

A different anhydride was also tried as a peroxy acid precursor. 2-Sulfobenzoic acid cyclic anhydride (SBCA) could potentially be a better reagent, since the sulfoxide anion is a better leaving group for the perhydrolysis reaction than the carboxylate. Under similar conditions, however, SBCA produced much less epoxide than the phthalic anhydride reactions. One explanation for this would be that the anhydride is reacting faster with the hydrogen carbonate, forming the salt, rather than reacting with the hydrogen peroxide and forming the peroxy acid. Once the salt is formed, it will be unreactive toward the peroxide. Other evidence for this is the fact that the yield of epoxide decreases with the increasing amount of sodium hydrogen carbonate, and the reaction is completely shut down when excess hydrogen carbonate is used.

Epoxidation of olefins by peroxy acids using nitriles and $\text{H}_2\text{O}_2 / \text{HCO}_3^-$

Nitriles can undergo perhydrolysis in alkaline solution to yield peroxyimidic acids. We decided to compare the sodium hydrogen carbonate system with sodium hydroxide, under similar conditions. The nitrile selected was acetonitrile, which will function as both reagent and solvent. Cyclooctene (5 mmol) was dissolved in 5 mL of acetonitrile. In a separate vial, 5 mmol of sodium hydrogen carbonate was added to 1 mL (20 mmol) of 70 % hydrogen peroxide. The two solutions were mixed to start the reaction. A similar reaction was setup where 5 mmol of NaOH replaced the sodium hydrogen carbonate. Decomposition of the hydrogen peroxide was evident at the moment the NaOH was added. After 20 minutes there was no peroxide left, as indicated by a starch iodide indicator paper. The results of the two runs are displayed in Table 3.7. The reaction

Table 3.6. Epoxidation of olefins using acid anhydrides as precursors.

Anhydride	Solvent	H ₂ O ₂	HCO ₃ ⁻	Olefin	Reaction Time (min)	Epoxide Yield (± 5 %)
PA, 5 mmol	MeOH 10 ml	10 mmol	Na ⁺ 5 mmol	cyclooctene, 5 mmol	90	72 %
PA, 5 mmol	MeOH 10 ml	10 mmol	-----	cyclooctene, 5 mmol	90	25 %
PA, 5 mmol	CH ₂ Cl ₂ 10 ml	10 mmol	Bu ₄ N ⁺ 5 mmol	cyclooctene, 5 mmol	30	67 %
SBCA, 5 mmol 	MeOH 10 ml	34 mmol	Na ⁺ 1 mmol	cyclooctene, 5 mmol	90	14 %
SBCA, 5 mmol 	MeOH 10 ml	34 mmol	Na ⁺ 5 mmol	cyclooctene, 5 mmol	90	1 %
SBCA, 5 mmol 	MeOH 10 ml	34 mmol	Na ⁺ 10 mmol	cyclooctene, 5 mmol	90	-----

using hydrogen carbonate is slower, due to the low solubility of the salt, but the hydrogen peroxide is not decomposed as in the hydroxide case, leading to better yields.

Table 3.7. Epoxidation of olefins using nitriles as peroxy acid precursors.

Nitrile	H ₂ O ₂	Base	Olefin	Reaction Time (min)	Epoxide Yield (± 5 %)
CH ₃ CN, 5 mL	20 mmol	NaHCO ₃ , 5 mmol	cyclooctene, 5 mmol	120	25 %
CH ₃ CN, 5 mL	20 mmol	NaOH, 5 mmol	cyclooctene, 5 mmol	20	9 %

Conclusions

The choice of conditions and reagents is of fundamental importance for the succesful transformation of unsaturated compounds into epoxides. When generating the active species *in situ*, special care must be taken to control the acidity of the medium. The method presented here for the perhydrolysis of peracid precursors in alkaline media succesfully generates the active oxidant while preserving the epoxide ring from acid catalysed opening.

The method presents advantages when compared to reacting the carboxylic acid directly with hydrogen peroxide. In the case of weak or moderate acids, a strong acid catalyst must be added to promote the peracid formation. When a strong acid is used, it will not need the extra acid catalyst, but in either case the yields of epoxide suffer from the

acidity. The only acceptable case where the presence of the acids is not a major drawback is in the epoxidation of unsaturated soybean oil. In this case the thick oil forms a separate phase with epoxidation taking place at the interface. Epoxide losses due to the aqueous hydrogen peroxide and carboxylic acid are small in this case. In the method presented here, the reaction starts with the ester of a strong carboxylic acid and the medium is neutral. As the reaction proceeds the acid generated is buffered by the basic promoter.

If the reaction was run in similar conditions but starting with the carboxylic acid (e.g. formic acid), neutralization would take place first and the corresponding salt would be unreactive toward hydrogen peroxide. When the ester is used, perhydrolysis occurs before neutralization of the acid, which allows the epoxidation to proceed.

The co-products of the reaction of the ester are the respective carboxylic acid and alcohol. Under the right conditions these may be recycled back to the ester. More work is necessary to establish ideal conditions for different types of olefins.

APENDIX

Time Course of Epoxide Formation

Epoxidation reactions were sampled along the reaction time. The conversion of the olefin to epoxide in different times is presented here for some reactions.

Methyl Formate

Epoxidation of allyl alcohol

Reaction Conditions:

Allyl alcohol - 5 mmol

Sodium hydrogen carbonate - 1 mmol

Methyl formate - 5 mL

Hydrogen peroxide - 34 mmol

Room temperature

Time (min)	Olefin Conversion	Epoxide Yield ($\pm$ 5 %)
30	2 %	2 %
60	5 %	5 %
180	8 %	8 %
1440	50 %	49 %

Epoxidation of cyclooctene

Reaction Conditions:

Cyclooctene - 5 mmol

Sodium hydrogen carbonate - 1 mmol

Methyl formate - 5 mL

Hydrogen peroxide - 34 mmol

Room temperature

Time (min)	Olefin Conversion	Epoxide Yield ($\pm$ 5 %)
30	73 %	70 %
60	90 %	87 %
90	98 %	95 %

Methyl TrifluoroacetateEpoxidation of 1-octene

Reaction Conditions:

Cyclooctene - 5 mmol

Sodium hydrogen carbonate - 1 mmol

Methyl formate - 5 mL

Hydrogen peroxide - 34 mmol

Room temperature

Time (min)	Olefin Conversion	Epoxide Yield ($\pm$ 5 %)
30	20 %	9 %
45	24 %	10 %
120	44 %	25 %

Phthalic AnhydrideEpoxidation of cyclooctene

Reaction Conditions:

Cyclooctene - 5 mmol

Sodium hydrogen carbonate - 5 mmol

Methanol - 10 mL

Hydrogen peroxide - 10 mmol

Room temperature

Time (min)	Olefin Conversion	Epoxide Yield ($\pm 5\%$)
15	57 %	52 %
30	67 %	62 %
60	70 %	65 %
90	76 %	72 %

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BIOGRAPHICAL SKETCH

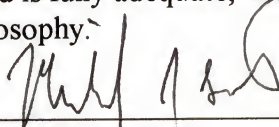
Alfredo Luis M. L. Mateus, son of Mario Joaquim Mateus and Emilia Maria Martins Mateus was born on September 21, 1967, in São Paulo, Brazil. He graduated from the University of São Paulo with a Bachelor of Science (Chemistry) in 1989. He received a master's degree in Inorganic Chemistry from the University of São Paulo in 1993. In the fall of 1993 he started a doctoral program in chemistry at the University of Florida under Graduate Research Professor Russell S. Drago. As a graduate student, he has contributed to the publication of two articles in major scientific publications and is currently preparing a third one.

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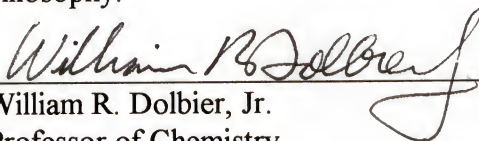
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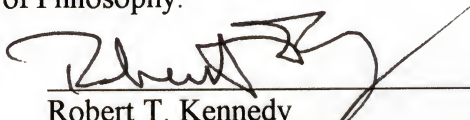
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This dissertation was submitted to the Graduate Faculty of the Department of Chemistry in the College of Liberal Arts and Sciences and to the Graduate School and was accepted as partial fulfillment of the requirements for the degree of Doctor of Philosophy.

August, 1998

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